Archives of Dermatology and Syphilology

VOLUME 33 FEBRUARY 1936 NUMBER 2

HISTIOCYTOMA CUTIS

FRANCIS E. SENEAR, M.D.
AND
MARCUS R. CARO, M.D.
CHICAGO

The rôle of the reticulo-endothelial cell in many medical disorders has received increasing attention in recent years, and perhaps in no field has it modified the conception of various diseases more than in dermatology. It is thought by many observers that the evolution of this cell is responsible for the development of the granulomas of mycosis fungoides, Hodgkin's disease and the cutaneous leukemias, and it is generally conceded now that the xanthoma cell is a histiocyte modified by the storing of cholesterol esters.[1] We have stated elsewhere [2] that the tumors of nevoxantho-endothelioma, first described by McDonagh, consist of modified histiocytes and that these lesions represent merely a form of juvenile xanthoma.

Recently we became interested in the rôle of the histiocyte in the production of a common and generally recognized tumor which has received relatively little attention in the literature. This is the lesion described by Unna [3] in 1896 as fibroma simplex and by Arning and Lewandowsky [4] in 1911 as noduli cutanei. Schreus [5] in 1930 stated that there had been no subsequent reports on the subject and added a report of three cases. He was in complete accord with Arning and Lewandowsky as to the clinical and histopathologic changes and proposed the name dermatofibroma lenticulare. Willbrand [6] in 1932 reported four more cases of the disorder and confirmed the recorded observations, as

From the Department of Dermatology, University of Illinois College of Medicine.

Read at the Fifty-Eighth Annual Meeting of the American Dermatological Association, Inc., White Sulphur Springs, W. Va., May 2, 1935.

1. Plewes, L. W.: Nature and Origin of the Xanthoma Cell, Arch. Path. **17**:177 (Feb.) 1934.

2. Senear, F. E., and Caro, M. R.: To be published.

3. Unna, P. G.: The Histopathology of the Diseases of the Skin, translated by Norman Walker, Edinburgh, W. F. Clay, 1896, p. 836.

4. Arning, E., and Lewandowsky, F.: Noduli cutanei, Arch. f. Dermat. u. Syph. **110**:3, 1911.

5. Schreus, H. T.: Dermatofibroma lenticulare, Arch. f. Dermat. u. Syph. **161**:456, 1930.

6. Willbrand, L.: Noduli cutanei oder Dermatofibroma lenticulare, Dermat. Wchnschr. **95**:1676, 1932.

did Gulden [7] in 1934. Other names used have been fibroma durum and *fibrome en pastille* (Civatte).

Traub and Monash [8] in 1932 described two cases and reported the observation of eight others. The condition in the two cases described by them resembled Boeck's sarcoid clinically to such an extent as to lead several dermatologists of experience to make that diagnosis erroneously. In the same year Michelson [9] reported a study of lesions of this type and, believing the growths to be of inflammatory origin, suggested the name nodular subepidermal fibrosis. He called attention to the fact that in recent lesions the number of connective tissue cells is greatly increased, producing a decidedly fibrosarcomatous appearance.

The fibrotic nodules occur as a rule on the extremities, especially on the legs, and may appear on other parts of the body. The number varies from one to twenty, but usually only one is present. The nodules vary in size from 1 mm. to 1 cm. in diameter, and are rarely larger. They are very hard, are round or spherical and in most instances are embedded in the skin with little or no projection above the surface, in a few cases causing an actual depression. The lesions are freely movable over the subcutaneous tissue, while the skin over them is adherent, smooth, as a rule, and in some instances slightly scaly. The skin overlying early lesions may be pinkish, but that over the older and characteristic growths is deep red, brownish red, yellowish or even ivory. Subjective symptoms are usually lacking, although occasionally slight itching or tenderness may be noted.

On histologic examination all the authors noted changes in the fibrous tissue responsible for producing the lesions observed clinically.

Unna distinguished histologically two forms of fibroma simplex: the diffuse and the circumscribed. In the diffuse type there was a great increase in the embryonic cellular collagenous tissue, which was nestled about the preserved blood vessels, glands and follicles so that these organs appeared to be directly embedded in the new tissue. At the margins the tissue became more cellular and passed finally into mantles of spindle cells about the neighboring blood vessels. In the circumscribed form the tumor was more sharply defined and was composed of avascular and moderately cellular coarse collagen bundles, which crossed each other at all possible angles and pressed the hair follicles, ducts and glands to the side.

Lewandowsky noted a circumscribed zone in the corium in which the collagen fibers were narrow, densely packed and intertwining and

---

7. Gulden, K.: Dermatofibroma lenticulare, Dermat. Ztschr. **68**:118, 1934.

8. Traub, E. F., and Monash, S.: Dermatofibroma, Arch. Dermat. & Syph. **26**:250 (Aug.) 1932.

9. Michelson, H. E.: Nodular Subepidermal Fibrosis, Arch. Dermat. & Syph. **27**:812 (May) 1933.

were separated by the many spindle-shaped cells. In places the cells were clumped together, suggesting the structure of a fibrosarcoma. Elastic fibers were not present.

Schreus, Willbrand and Gulden observed histologic changes which were identical. There was a horizontal circumscribed fibrous area in the corium separated from both the epidermis and the hypoderm by a zone of normal tissue. Within this zone the collagen tissue was transformed into narrow spindle-shaped bundles, which at times were parallel with the epidermis but were mostly irregular and whorl-like. There was a great increase of spindle-shaped connective tissue cells. Elastic fibers disintegrated when they entered this area, and there was almost entire absence of elastic fibers within the area. There was no sharp separation of the lesion from the surrounding tissues.

Traub and Monash also described densely packed fibrous tissue in the subpapillary part of the corium, which only occasionally extended up into the papillae to produce flattening of the epidermis. In eight of their ten cases there was absence of elastic fibers in the tumor.

Michelson observed the principal changes to be confined to the corium. The collagen bundles were thickened, ran in wavy lines and had a homogeneous appearance. In young lesions the number of connective tissue cells was greatly increased, to suggest a fibrosarcomatous appearance, while in older lesions there were practically no nuclei, the lesion being made up of a clear homogenized mass looking like a compact mature scar. Elastic fibers were almost entirely absent. Hair follicles, sebaceous glands and sweat glands were lacking in the lesion, and lymph spaces and blood vessels were compressed within it. At the periphery of the nodule the vessels were thickened and sclerosed.

In common with others, we have observed many patients with lesions of this type and have had occasion to remove a number of the lesions. Several years ago sections of lesions from one patient were stained with sudan III, and it was noted that many of the cells were filled with lipoid droplets. After this observation, we carried out stains for fat on all lesions of this type and discovered that intracellular fat was present in a large proportion of cases. As this observation had not been recorded in any of the aforementioned articles, we made a search of the literature in an attempt to find an explanation, and in this way we were led to the observations of Woringer and other French dermatologists, notably those of the Strasbourg school.

Woringer,[10] at the réunion dermatologique de Strasbourg in 1931, called attention to the presence of histiocytes in nodules commonly accepted as fibromas. He pointed out that the cells of fibroma never

10. Woringer, F.: Histiocytoma of the Leg, Bull. Soc. franç. de dermat. et syph. **38**:1401, 1931.

become charged with fat, while in many of the lesions under consideration the tumor consisted of histiocytic cells filled with lipoids. In 1932 Woringer and Kwiatkowski [11] stated that the term histiocytoma is not often found in the classification of cutaneous tumors, a diagnosis of fibroma generally being made. They stated that histiocytomas are small tumors which appear insidiously in healthy adults, increase in size slowly over a period of years and in general remain stationary after reaching a certain size. Sometimes there may be rapid growth after more or less prolonged stationary periods. The lesions usually occur on the limbs but also develop on the trunk. They are single or multiple, usually small, from the size of a cherry pit to that of an almond or larger. The small lesions are level with the surrounding skin and hard and involve the entire corium, with the greatest development in its depth. The lesions are not adherent to the underlying tissues, are sharply demarcated and are especially appreciable on palpation. Symptoms are lacking. The lesions may be removed surgically without recurrence.

It will be seen that the clinical description is in the main the same as that of the fibroma. The only conclusive differential point, according to Woringer and his associate, is the absence of fat-infiltrated cells in the fibroma, since only the histiocyte is capable of taking up fat.

The authors also called attention to certain characteristics which cause the histiocytoma to resemble the cutaneous xanthoma. The lesions of the latter disorder are characterized by the abundance of xanthoma cells, i. e., histiocytes the protoplasm of which is so filled with lipoids that they form typical foam cells. In xanthomatous lesions one may find also groups of fusiform cells, which are histiocytes the protoplasm of which is not yet charged with fatty deposits. The authors expressed the opinion that the histiocytoma is directly related to the xanthoma, as the histiocyte is the parent cell in both and lipoid infiltration occurs in both. In the fibroma, on the other hand, the cell of origin is the fibroblast, which is capable of elaborating collagen but incapable of undergoing vital staining. It is possible, however, according to Pautrier and Woringer,[12] that in some instances histiocytoma may be observed before infiltration by fats has occurred, in which circumstance it would be impossible to identify it with certainty.

Sézary and Lévy-Coblentz [13] also reported three cases of this condition. In their first case they observed only fusiform cells occurring

11. Woringer, F., and Kwiatkowski, S. L.: Histiocytoma of the Skin, Ann. de dermat. et syph. **3**:998, 1932.

12. Pautrier, L. M., and Woringer, S. L.: Histiocytoma of the Skin, Bull. Soc. franç. de dermat. et syph. **40**:1659, 1933.

13. Sézary, A., and Lévy-Coblentz, G.: From Histiocytoma to Xanthoma, Bull. Soc. franç. de dermat. et syph. **40**:798, 1933.

in bundles arranged in whorls, while in the second there were also some spongy cells, fusiform or rounded, with one or several nuclei, some forming cells of the Chambard type. There were all forms of transition from the fusiform to the spongy type of cell, the latter being the end-result of a process of lipoid surcharge. In their third case the authors regarded the picture as frankly xanthomatous. They therefore expressed the opinion that it is possible to regard the three cases as representing a transition from a simple histiocytoma to true xanthoma. In the first case the condition is to be regarded as pure histiocytoma, in the second as histiocytoma with xanthomatous changes and in the third as xanthoma. In the different sections it was possible to demonstrate fusiform cells in the process of becoming infiltrated with cholesterol, some containing only traces and not being deformed, while others, with larger amounts, were becoming globular and were undergoing transformation into cells of the Chambard type.

Sézary and Lévy-Coblentz,[14] in replying to a criticism that the tumors which they had described were in reality fibromas, reported two cases which they had studied and in which they had made the diagnosis of fibroma. They admitted that in most cases the clinical differences between fibroma and histiocytoma are not conclusively diagnostic. Fibroma is more often multiple, while histiocytoma is usually a solitary tumor. A predilection for the extremities is common to both, and the factors of age and sex of the patient are of no importance. From the histologic standpoint, the authors state that in some instances the differentiation is easy, while in others it is difficult. They observed that in the fibroma the tumor cell is the fibroblast, a fusiform or branching cell, with a fibrillar or clear protoplasm and with a spindle-shaped nucleus. There is little variation throughout the tumor. All the fibroblasts have a nucleus and protoplasm of identical aspect, and they are separated by fine collagenous lamellae. In the histiocytoma, on the other hand, while the fundamental cell is also a fusiform cell, which is likely to anastomose and to form bundles and whorls, the spindle is short and thick, and the cell is richer in protoplasm. The nuclei are larger and less regular than in the cells of fibroma. Finally, the cells sometimes form irregular clusters or are packed one against another without regular interposition of the collagenous lamellae.

To these morphologic differences must be added an important biologic distinction. The histiocyte has the property of taking up various substances, among which are most often the lipoids and the ferric pigment with origin in the blood. The storage of these substances modifies greatly the appearance of the histiocyte; the cells become more or less

14. Sézary, A., and Lévy-Coblentz, G.: Fibroma En Pastille and Histiocytoma, Bull. Soc. franç. de dermat. et syph. **40**:1269, 1933.

globular and in some instances assume the form of multinucleated giant cells. The fibroma cell is incapable of these changes. In Sézary and Lévy-Coblentz' patients with fibroma, even when hypercholesteremia was present, the tumor cells showed no inclusion of lipoids, as the fibroblast is limited to its fibroblastic function and lacks the plasticity and phagocytic activity of the histiocyte.

Civatte,[15] in discussing the report of Sézary and Lévy-Coblentz, agreed with them as to the existence of histiocytomas but stated that it is generally conceded that the fibroblast is evolved from the histiocyte. It is capable of elaborating collagenous tissue but unable to recover the plasticity which characterized it in its previous state and cannot resume the functions of the histiocyte. Civatte expressed the opinion, therefore, that the histiocytoma may be looked on as a fibroma arrested in its evolution.

Pautrier and Woringer[12] replied to this criticism by pointing out that the biologic difference between the types of cells is specific. The ability to fix colloids is never present in cutaneous fibroma, in fibroma of the ovaries or in dermatofibrosacroma protuberans but is never wanting in histiocytoma. They advocated the use of the term histiocytoma for those lesions in which the infiltration with lipoids is relatively slight and xanthoma for those in which the cells are surcharged with lipoids, producing cells of the Chambard type.

Massia and Pillon[16] also described a case of histiocytoma in which the lesion clinically resembled fibroma. Microscopically the cells presented the frothy aspect of the xanthoma cell.

Michel and Morel[17] reported a case which was of interest because of the appearance and site of the growth. The patient was a man aged 50 years, who presented in the left nasogenial fold a rounded projecting tumor the size of a pea, of hard consistency, having a broad base, suggesting the diagnosis of nevus. The lesion had appeared six months before and had grown slowly. It was histologically a characteristic histiocytoma. Removal with the galvanocautery was followed by a recurrence of the tumor nine months later. Milian and Perin[18] and Weissenbach, Cailliau and Martineau[19] recently described cases of tumors of this type.

---

15. Civatte, in discussion on Sézary and Lévy-Coblentz.[14]

16. Massia, G., and Pillon, M.: Histiocytoma of the Flank, Bull. Soc. franç. de dermat. et syph. **40**:1083, 1933.

17. Michel, P. J., and Morel, H.: Neviform Histiocytoma of the Naso-Genial Fold, Bull. Soc. franç. de dermat. et syph. **40**:1084, 1933.

18. Milian, G., and Perin, L.: Histiocytoma of the Skin, Bull. Soc. franç. de dermat. et syph. **40**:555, 1933.

19. Weissenbach, R. J.; Cailliau, F., and Martineau, J.: Histiocytoma of the Skin, Bull. Soc. franç. de dermat. et syph. **42**:344, 1935.

The benign character of the histiocytoma has been emphasized by all observers, but Dupont [20] described what he believed to be an example of a malignant form. His patient was a woman, 33 years of age, who presented on the posterior aspect of the thigh a slowly growing tumor of two years' duration, with the appearance of a malignant melanoma. The growth was removed by means of electrocoagulation, which was followed by radium therapy. Two chief types of cells were observed in the sections. The first was a fusiform cell, with the shape of a young fibroblast. The second was a large cell containing either a single but distorted nucleus or atypical multiple nuclei of unequal size, arranged without order either at the center or at the periphery of the cell. Frozen sections showed abundant doubly refractile oily droplets. Dupont stated that the clinical appearance was typically that of a histiocytoma. The extreme irregularity of the form and structure of the cells and the multiple nuclear monstrosities were the basis for his opinion that the tumor was malignant. He expressed the opinion that the lesion bears the same relation to histiocytoma as fibrosarcoma does to fibroma.

CLINICAL DESCRIPTION

We have studied twenty-five cases, all of them occurring in white persons. Of these, six were in males and nineteen in females. The age of the patients varied from 17 to 55 years. The most recent lesions had been present for about four months, while several had been present for at least ten years. The onset was usually insidious and unnoticed. In several cases there was definite knowledge of an injury to the skin preceding the onset, as in the case of a patient in whom a lesion appeared on each leg at the site of a hypodermic injection and of another in whom a nodule appeared after an insect bite on the leg. In most cases, however, no preceding injury or local inflammation could be remembered. There were no symptoms in any of the cases to direct the patient's attention to the lesion, the patient being unaware of its presence in several instances. The rate of growth was very slow and hardly appreciable, and spontaneous involution of the tumors was not observed. Excision was not followed by the formation of a keloid, and in no case were there associated keloids.

In our cases lesions were present on various parts of the body, but they occurred most frequently on the extremities, especially on the legs, and on the shoulders. A single lesion was present in most cases, and in only four were there multiple lesions. They varied in size from 1 mm. to 2 cm., were round or ovoid and varied in color from a light grayish brown to a deep violaceous red, some nodules showing a definitely

20. Dupont, A.: Malignant Histiocytoma of the Skin, Bull. Soc. franç. de dermat. et syph. **40**:674, 1933.

yellowish hue. The surface in general was smooth and shiny, but occasionally it was roughened and showed a slight peripheral scale. The consistency was of a woody hardness and in most instances gave the impression of a firm disk inserted into the skin and attached to it (fig. 1). The sharp circumscription and separation from the surrounding skin

Figure 1

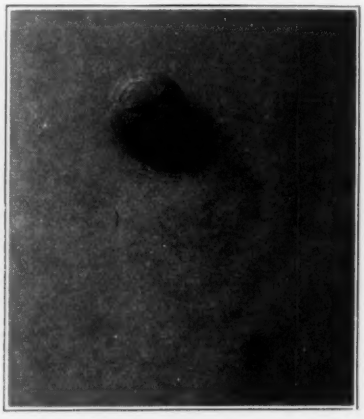

Figure 2

Fig. 1.—The nodule above the knee shows the usual appearance of a histiocytoma cutis.

Fig. 2.—The large histiocytoma cutis shows more elevation above the surface than is common.

Fig. 3.—The nodule is sharply circumscribed and shows an abrupt elevation from the skin.

could be palpated rather than seen. Most of the lesions were level with the skin, showing a slight depression at the border and only a slightly arched elevation in the center. A few larger ones, however, showed an abrupt elevation at the border to form an exteriorized tumor up to 1 cm. in height, resting on a sessile base and resembling a keloid in appearance (figs. 2 and 3). Pedunculation of the base was never observed. The

skin could not be moved over the lesion, but the nodules were freely movable over the deeper structures and could be readily picked up.

In three cases chemical examination of the blood showed the cholesterol content to be, respectively, 151, 156 and 179 mg. per hundred cubic centimeters of blood, all of the results being within normal limits.

HISTOPATHOLOGY

The histologic observations on nodules from different cases disclosed differences of degree which, rather than differentiating them, helped to explain their progress through the several stages of development.

In a biopsy specimen taken from a young and small lesion (hemalum-eosin stain) the epidermis was normal (fig. 4). The papillary layer showed no change except for dilatation of the blood vessels and a slight perivascular infiltration of lymphocytes and histiocytes. In the lower two thirds of the corium the normal structure was invaded by a poorly circumscribed mixture of cells and pale fibers. Separating the remnants of the preexisting collagen fibers, the invading fibers lay in narrow wavy strands, which intertwined in various directions and occasionally formed whorls. Between the fibers lay rows of cells with spindle-shaped, ovoid and occasionally rounded pale nuclei. The greatest number of cells occurred in the center of the whorls, while in other areas the fibers were relatively acellular. A few sweat glands remained within the fibrous mass as well as several blood vessels, and the adventitial cells of the latter were indistinguishable from the invading cells. At the sides there was an irregular outward extension of the fibers, and mantles of similar cells accompanied the vessels and sweat glands. A pilosebaceous organ was present on each side. A narrow zone of normal corium separated the lesion from the hypoderm. With the Van Gieson stain the new fibers were stained poorly while the Weigert stain showed the elastic fibers to be normal in the upper third of the corium and still present below as wavy strands and short fragments between the invading fibers. No lipoid droplets were seen (sudan III stain), and examination with the polariscope showed no doubly refracting crystals.

A larger and older papule showed similar but more advanced changes (fig. 5). The epidermis was acanthotic, and there was dilatation of the vessels in the papillae. The entire corium was filled with fibrous tissue, which extended up to the papillae. The mass was densely packed and very cellular. The cells were large and pale and for the most part had large ovoid and rounded nuclei. In some areas there were wavy strands of parallel fibers, intertwining in many directions and containing rows of slender spindle-shaped cells. Toward the center there were a few ill defined homogeneous acellular fibrous areas. No blood vessels, glands or hair follicles were observed within the lesion.

Fig. 4.—The upper part of the corium contains dilated vessels, while the lower part is invaded by intertwining fibrous bundles. Hemalum-eosin stain; × 90.

At the sides, however, lay several hair follicles, sebaceous glands and thickened vessels, and below were many thickened vessels surrounded by an infiltrate of histiocytes and lymphocytes. Collagen fibers stained poorly, and elastic fibers were not present within the nodule. Staining with sudan III (fig. 7, upper section) disclosed many lipoid droplets within the cells throughout the lesion, and examination with the polariscope revealed the tissue to be filled with doubly refracting crystals.

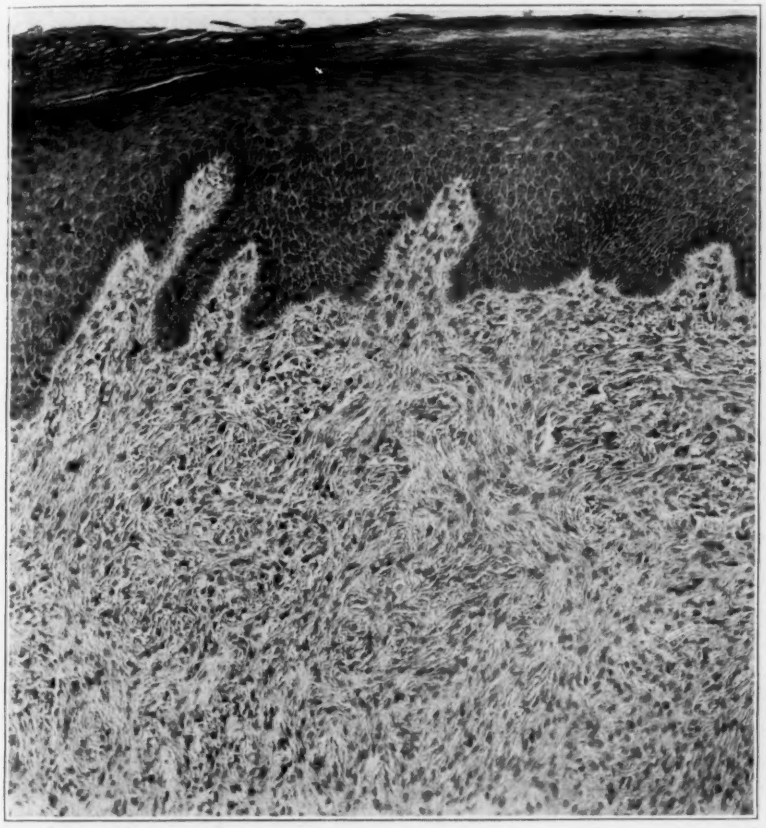

Fig. 5.—The cellular fibrous tissue extends up to the epidermis. Hemalum-eosin stain; × 90.

In another elevated nodule the epidermis was flattened (fig. 6). The papillary layer was replaced by a narrow zone of densely packed horizontal fibers and ovoid and spindle-shaped cells and contained many dilated thin-walled blood vessels. The underlying corium was filled with a densely packed cellular mass. Most of the cells were large and rounded and had a large round or ovoid pale nucleus, with a small dark nucleolus. The cells showed great variation in size, and in many there were several

clumped nuclei. Throughout there were many small thin-walled vessels, the walls of which seemed continuous with the surrounding cells. There was no sharp border around the nodule. At the periphery the cells became more elongated and even spindle-shaped, and there were more distinct bundles of intercellular fibers. The underlying vessels were surrounded by edematous mantles of histiocytes and lymphocytes. A few strands of deeply stained collagen fibers were still present within

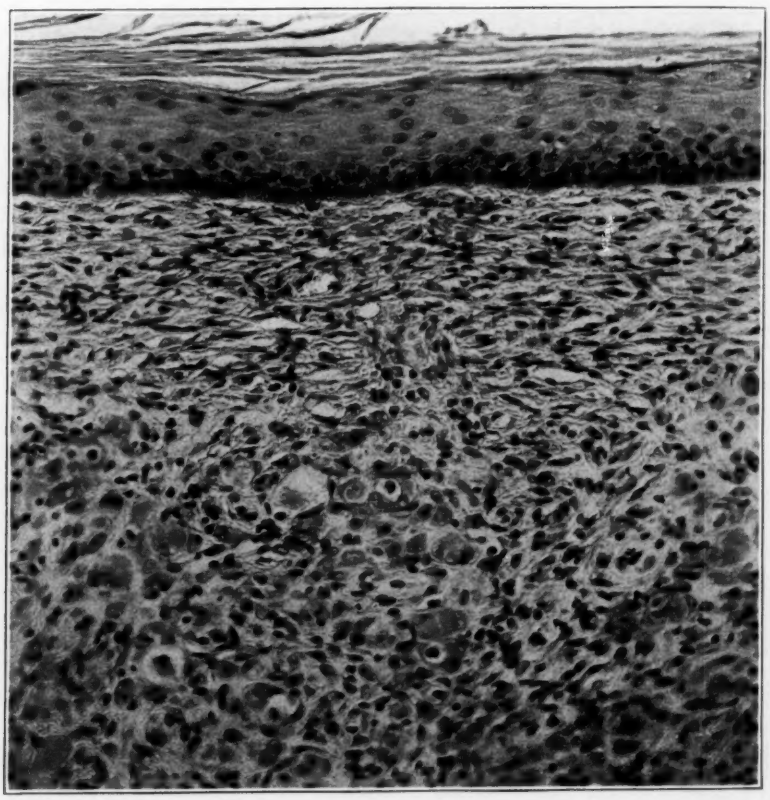

Fig. 6.—The epidermis is flattened; below it lies a narrow zone of horizontal fibers which separates it from a large mass of densely packed histiocytes. Hemalum-eosin stain; × 180.

the lesion, but elastic fibers were lacking. No sudanophilic droplets or doubly refracting crystals were noted.

In an older tumor the epidermis was thin and flattened. The entire corium was filled with a densely packed fibrous mass in which the fibers were pale and more homogeneous and were separated by fewer and flatter dark-staining cells (fig. 8). In some areas there remained clumps of larger cells with pale vesicular nuclei. No structures remained within

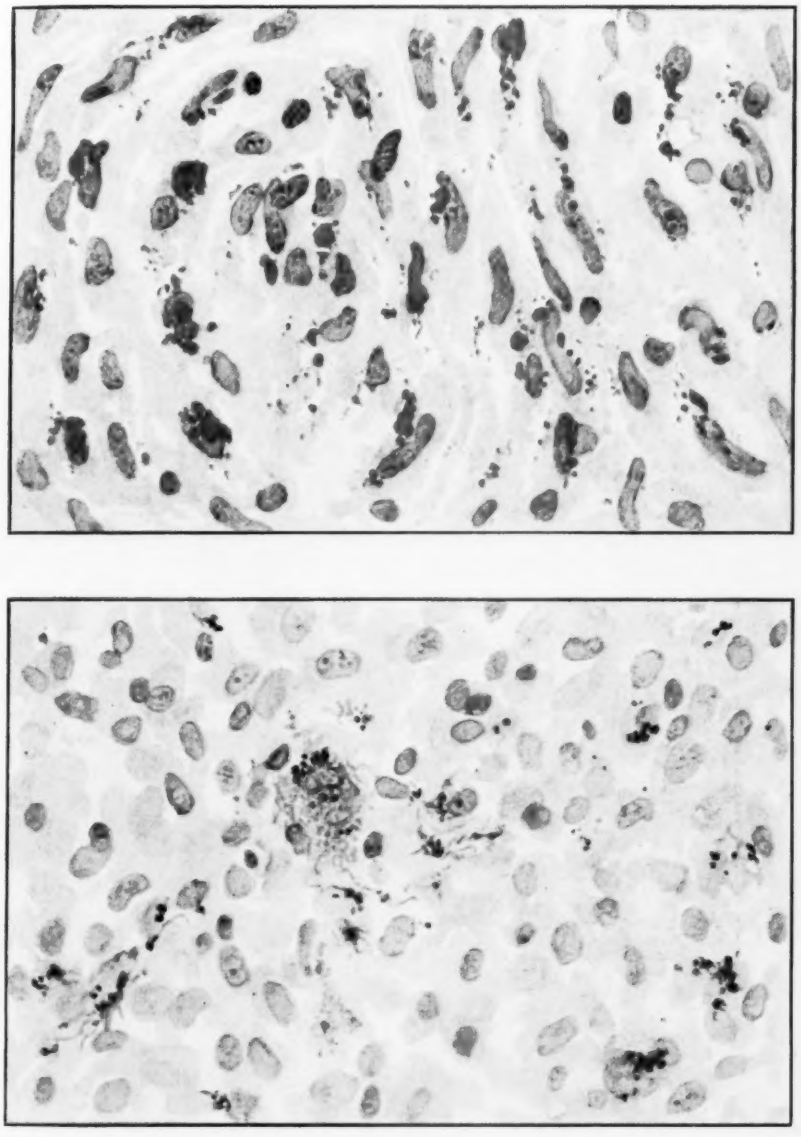

Fig. 7.—The upper section shows many of the histiocytes with intracellular droplets of sudanophilic lipoids. Sudan III stain. The lower section shows granules of iron within the cytoplasm of many of the histiocytes. These granules were taken up by the cells following the subcutaneous injection of an aqueous solution of saccharated ferric oxide. Perl's prussian blue reaction.

UNIV. OF MICH.

the mass except the dilated blood vessels near the surface, and the hair follicles and sweat glands were pushed to the side. There was no sharp line of demarcation about the nodule, and edematous mantles of cells extended laterally and downward about the blood vessels. Many well stained collagen fibers coursed through the nodule, but elastic fibers were entirely lacking. Many intracellular sudanophilic lipoid droplets were present in the cellular areas, and on examination with the polariscope a few doubly refracting crystals were observed.

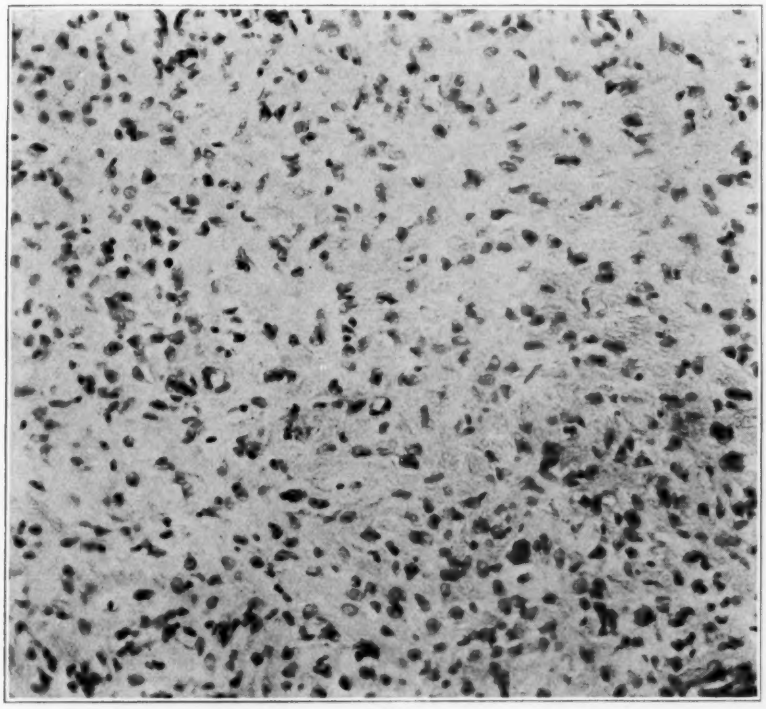

Fig. 8.—Dense fibrous tissue, with relatively few cells, taken from an older lesion. Hemalum-eosin stain; × 180.

The histologic changes in biopsy specimens taken from the patients in all twenty-five cases corresponded to those described earlier. In fifteen cases staining with sudan III demonstrated the presence of intracellular lipoid droplets, and in all of these examination with the polariscope revealed the presence of doubly refracting crystals.

To discover the nature of the cells composing the tumors we made use of a test for the vital staining of cells by the storing of colloidal iron. In the last five cases of our series (six lesions) a few drops of a 10 per cent aqueous solution of saccharated ferric oxide was injected under

the nodule. Two days later the lesions were excised, prepared in the usual manner and stained for iron (Perl's test for reaction to prussian blue). In all six lesions it was noted that granules of iron had been taken up by the cells. Intracellular granules of iron could be demonstrated clearly in many cells, being more numerous in cells near the bottom, close to the site of the injection, but present also within cells far toward the center of the nodules (fig. 7, lower section). This was conclusive proof that the cells in question were histiocytes, for only those cells have the biologic function of taking up foreign material.

PATHOGENESIS

There has been a good deal of controversy about the mode of production of the lesions and about the origin of the parent cells. Unna and Arning and Lewandowsky considered the nodules to be simple fibromas. More recently Schreus and other German authors and Traub and Monash have expressed their belief in a similar fibroblastic origin. Michelson also stated that the lesions are derived from fibroblasts but are inflammatory rather than true tumors.

We differ completely from these views and agree fully with Woringer and other French authors that the cell of origin in the tumors is the histiocyte rather than the fibroblast. The presence of lipoids within the cells is good evidence of this, for under ordinary conditions only histiocytes have the ability to take up lipoids. We cannot agree with Pautrier and Woringer, however, in their statement that only the histiocyte can store lipoids, for we have demonstrated the presence of sudanophilic lipoid droplets and of doubly refracting crystals within the cells of dermatofibrosarcoma protuberans and of fibrosarcoma.

We have been able to add what we believe to be conclusive proof, however, of the histiocytic nature of the cells by vital staining with colloidal iron. The storage of granules of iron by the cells composing the tumor proves beyond a doubt that the cells are a part of the reticuloendothelial system, for no other cells are capable of this function.

One may state, as did Civatte, that in a broad sense a histiocytoma is a fibroma arrested in evolution, for it has been shown repeatedly, especially in tissue cultures, that histiocytes may become transformed into fibroblasts. It is wrong, however, to consider the two tumors as being identical. A fibroma is a static tumor derived from highly differentiated cells. A histiocytoma, on the other hand, is derived from comparatively labile cells, and it is subject to many changes under the influence of the rest of the body. It is this susceptibility to outside influences that accounts for the varied histologic observations in different cases.

Even though we can trace the progress of the changes that produce the tumor, it is difficult to state with certainty what initiates them in the

first place. In several of our cases there was a history of a definite injury to the site, such as the prick of a needle, an insect bite or a bruise. Other authors have mentioned preceding lesions, such as pustules and lichen planus papules, as being responsible for the development of the tumor. Since the lesion is free from symptoms and is never noticed at the onset, it may be possible that it is always preceded by some injury to the site too trivial to be noticed at the time or remembered later.

The first change is probably a proliferation of histiocytes about the blood vessels, for in the advancing border of a young nodule such perivascular changes are noted. The histiocytes proliferate and spread into the surrounding tissues and in their fibroblastic capacity produce narrow wavy bundles of fibers. In some lesions the histiocytes predominate, and a cellular nodule is formed. In older lesions the cells are compressed and overshadowed by the fibers, and dense homogeneous fibrous tumors result. If at some time during the formation of a tumor there should be an increase in the lipoid content or a disturbance in the lipoid partition of the blood, the histiocytes present in the tumor may become infiltrated by the lipoids to a varying degree. Nodules containing a slight amount of lipoids may result, and at times even lipoid-laden tumors, approaching the appearance and histologic structure of a xanthoma.

Although we have not observed an instance of spontaneous involution of a tumor in our series, other authors [21] have reported occasional spontaneous disappearance. While this would hardly be possible with a fibroma, involution is entirely within the scope of a histiocytoma. It is well known that xanthoma, which is also of histiocytic origin, may undergo complete involution. The same may be true of histiocytoma, which is less heavily infiltrated with lipoids.

The name histiocytoma cutis may be open to criticism by those who feel that we are dealing not with a true tumor of spontaneous origin but rather with inflammatory histiocytosis. The designation is appropriate, however, as being descriptive of the tumor-like appearance, the cutaneous site and the histiocytic origin.

DIFFERENTIAL DIAGNOSIS

The appearance of a histiocytoma cutis is usually sufficiently distinctive to enable one to make the correct diagnosis clinically. As with most cutaneous tumors, however, the exact diagnosis depends entirely on a histologic examination. The presence in the corium of a poorly defined zone of intertwining strands of fibers and pale histiocytes, especially when the latter contain lipoid droplets, is diagnostic. Vital staining of the cells by colloidal iron makes the diagnosis conclusive.

21. Ebert, M.: In discussion on Michelson.[9]

Fibroma is more often multiple and differs also in being more elevated and usually softer than histiocytoma. Fibrosarcoma grows more rapidly and shows more invasion of the surrounding and deeper tissues. In both, a histologic differentiation can be readily made.

Keloid and keloidal scar occur generally at the site of a known injury to the skin. They are hard, raised tumors that show an abrupt elevation from the skin and histologically show a preponderance of densely packed, parallel, thickened collagen fibers.

Xanthoma clinically is more yellowish and in most cases shows elevation of the tumor and multiplicity of lesions. Histologically the cells are infiltrated with a greater amount of lipoids, to produce the characteristic foam cells of Chambard or even the giant cells of Touton.

Pigmented nevus shows more elevation and generally a darker brown. Malignant melanoma is much darker, grows more rapidly and becomes elevated and at times ulcerated.

Sarcoid is seldom confused, for its softer consistency, more reddish color and characteristic tuberculous histologic changes are diagnostic.

TREATMENT

Surgical excision is the treatment of choice, and radiation therapy is never necessary. Incomplete excision is followed by a recurrence of the lesion, which, however, requires only more complete removal.

SUMMARY AND CONCLUSIONS

The skin offers an unusually available field for the study of the rôle of the histiocyte in the development of disease. As a result of many recent investigations of this cell, new conceptions of the pathogenesis of various diseases have been made possible. The origin of xanthoma and systemic lipoid granuloma has been attributed to changes in the cells of the reticulo-endothelial system, and it would appear that Hodgkin's disease, granuloma fungoides, the leukemias and possibly other related diseases may have the same source.

The study of the histiocyte has made possible a new interpretation of the common cutaneous tumor previously accepted, under its various names, as a fibroma. While pure fibroma of the skin may occur, it is probable that in the majority of cases with such a diagnosis the constituent cell is not a fibroblast but rather a histiocyte. The clinical differentiation of histiocytoma from fibroma is difficult. There are certain morphologic differences between the cellular elements which make a histologic differentiation possible in some, but not in all, cases. Definite identification of histiocytic tumors can be made, however, by the demonstration of cells which have the biologic function of the storing of electronegative colloids. The cells may have exercised this function by taking up lipoids, as demonstrated by staining with sudan III or by

a polariscopic examination. This property of the cells may be demonstrated more conclusively, however, by vital staining with colloidal iron.

Depending on the cellularity of the tumor and the variations in the lipoid content of the cells, the histopathologic picture may vary from that of a densely fibrous tumor to one presenting changes approaching those noted in a typical xanthoma.

We have studied twenty-five cases of lesions of this type. It was possible to demonstrate the presence of intracellular lipoids in the lesions in fifteen cases. In the three cases of the remaining ten in which we were able to perform the test of vital staining, the histiocytic nature of the cells was shown by the demonstration of intracellular granules of iron. It may be assumed that the condition could have been similarly identified in the remaining seven cases if we had been able to carry out the test.

Histiocytomas of the skin are exceedingly common and are frequently overlooked because of their insignificance and usual lack of symptoms. They offer an excellent field for the further investigation of the histiocyte in disease.

ABSTRACT OF DISCUSSION

Dr. H. N. Cole, Cleveland: Last week at the meeting of the Cleveland Dermatological Society a patient with a replica of the condition was presented by Dr. Connor and Dr. Sullivan from my service at the Cleveland City Hospital. I have seen quite a few cases in the past and have looked on the condition as a spontaneous type of keloid. This seemed to comply fairly well with the observations on histologic examination, for I noted the formation of what looked like fibrous or scar tissue. There was a little difference between it and the condition of the patient presented last week and that in the cases Dr. Senear has described, in that there were hypercholesteremia and what seemed to be the presence of characteristic foam cells; and it was decided that this was a case of fibroxanthoma. I should like to hear Dr. Senear's comments as to the relationship of this to histiocytoma.

Dr. J. Frank Fraser, New York: Dr. Senear has made a very valuable contribution. It is possible that many dermatologists may have been diagnosing the condition as neurofibroma.

Dr. Karl G. Zwick, Cincinnati: The substitution of colloidal mercury sulfide for the colloidal iron employed successfully by Dr. Senear and Dr. Caro might be a technical advantage in several respects and might facilitate analogous investigations. The dispersion of colloidal mercury sulfide is of high degree, but it may be varied almost at will by suitable manipulations. The mercury sulfide is insoluble in potassium bichromate, alcohol, formaldehyde, toluene and even sulfuric acid. Nearly all the ordinary fixing and staining reagents do not remove the mercury compound. Only the iodides (aqueous solution of iodine, U. S. P.) extract the mercury sulfide. As the examination of control sections is at times desirable, this solubility might serve a useful purpose. (Colloidal mercury sulfide is readily available; it is manufactured by The Hille Laboratories, Inc., Chicago. It has been reported on by the Council on Pharmacy and Chemistry of the Amer-

ican Medical Association [J. A. M. A. **92**:1349 (April 20) 1929] and is listed in "New and Nonofficial Remedies.")

Dr. Lloyd W. Ketron, Baltimore: I have examined histologically several of these tumors and have always considered them to be fibromas. Certainly the main part of the growth is composed of fibrous tissue. Does Dr. Senear believe that the fibrous tissue is derived from the local fixed undifferentiated mesenchymal cells found in small numbers in all connective tissue?

Histiocytes may be present in a variety of pathologic formations and reactions, and unless they can be definitely proved to be the parent cells of the fibrous tissue which predominates in the tumor, I do not see why one should call such formations histiocytomas in preference to fibromas.

Dr. D. L. Satenstein, New York: I see many tumors of this type at the New York Post-Graduate Medical School and Hospital. The patients are admitted with a diagnosis of fibroma and occasionally with a diagnosis of molluscum contagiosum. As a rule there is a single lesion. It is true that my associates and I may carry out some tests with vital staining if there is more than one lesion, but that is rare, and no one thinks of using the vital stains for one lesion. The histiocytes are probably the earliest cells, and the fibrous tissue is the result of a later reaction. Occasionally, the lesions go on to complete fibrosis, with only a few of the cells remaining at the margin. I have been calling the cells fibroxanthoma-like and have suggested that the patient be examined for cholesteremia. I do not know why Dr. Senear chose the name histiocyte instead of the other names given to the cells. If one puts them under the general term of reticulo-endothelial cell instead of histiocyte it would be much better.

Dr. F. E. Senear, Chicago: With regard to Dr. Cole's comment as to his having considered these lesions as keloids, we stated in the paper that we have watched in all the cases in which lesions have been excised for the development of keloids and have observed none, and we have looked for keloids in other areas of patients with the lesions but have found none. In several instances we have definite evidence of trauma preceding the lesion, as puncture with a hypodermic needle in one case and a mosquito bite in one, and in one case in the literature the lesions followed lichen planus papules. We were unable to find evidence of injury in the others but believe that the injury may have been so slight that the patient did not remember it.

Dr. Cole spoke of the presence of foam cells in his case. In some of the cases reported by other observers it has been stated that the cells in some instances cannot be differentiated from true foam cells.

Dr. Ketron asks why we should not continue to call these growths fibromas. Some of the lesions may consist entirely of fibroblastic cells and fibrous tissue and are true fibromas, but the vast majority of them are made up of thickly packed reticulo-endothelial cells. Eventually, as Dr. Satenstein stated, many of them progress to complete fibrosis.

Dr. Satenstein said that multiple lesions are extremely rare. I think that is questionable. We had eight cases in a group of twenty-five in which there was more than one lesion, and it would be possible therefore to use injections of different substances.

In the many papers written on the subject of the reticulo-endothelial cells, various names have been employed to designate them. We chose the term histiocytoma because the French dermatologists, who are the only ones dealing thoroughly with the subject, have used this term throughout, and we thought that the adoption of another name might lead to confusion.

PHENOLPHTHALEIN DERMATITIS

AN EXPERIMENTAL STUDY INCLUDING REPRODUCTION OF THE ERUPTION IN SKIN TRANSPLANTS

FRANK CROZER KNOWLES, M.D.
PHILADELPHIA

HENRY B. DECKER, M.D.
AND
ROSCOE P. KANDLE, M.D.
CAMDEN, N. J.

It has been said that "no synthetic drug has been introduced which has not in isolated cases given rise to symptoms of intolerance associated with cutaneous manifestations." [1] The truth of this statement is being constantly confirmed by a steadily lengthening list of articles on the subject, with an increasing number of incriminated drugs. The status of the older remedies being pretty well established in this respect, present-day literature on the subject is largely concerned with the newer preparations, especially those of synthetic origin.

It would seem that two factors are especially involved in the production of such reactions, namely, the quantity of the drug and the reaction of the human organism to its presence. As to the procedure involved, there are two important possibilities, either a form of hypersensitivity or a toxic process. If the former is the mode of production, the quantity of the drug used should have little effect, as the organism should react to an exceedingly minute dose as well as to an ordinary one. In the case to be cited it will be seen that the patient reacted very slightly to a small (not infinitesimal) dose and reacted typically only to a relatively larger, the usual therapeutic, dose. Primarily there must exist some idiosyncrasy on the part of the patient, since great numbers of people take such drugs, in many instances in large doses, without any reaction of the type to be described. The basis must be some abnormality of the individual patient, probably in the nature of hypersensitivity. If the observations on our patient are correct, persons reacting to phenolphthalein may, rarely, have a fluctuating idiosyncrasy, and lesions may

---

From the Department of Dermatology, Jefferson Medical College.

Read at the Fifty-Eighth Annual Meeting of the American Dermatological Association, Inc., White Sulphur Springs, W. Va., May 4, 1935.

1. Wright, C. S.; Wile, U. J., and Smith, N. R.: A Preliminary Study of the Experimental Aspects of Iodide and Bromide Exanthems, Arch. Dermat. & Syph. **6**:529 (Nov.) 1922.

disappear during further ingestion of the drug. This apparently occurred with our patient.

Broadly speaking, in most instances drugs cause a fairly typical cutaneous response in a person sensitive to them. These appearances have been adequately described and are usually easily recognized if one realizes the possibility of a drug as the etiologic agent.

Phenolphthalein in its typical effect causes a so-called fixed eruption. Only four other drugs are said to cause a similar type of outbreak: aminopyrine, the arsphenamines, antipyrine and allylisopropyl barbituric acid. The first recognition of the phenolphthalein eruption was reported by Abramowitz.[2] For details one may refer to the description given by Newman.[3]

Besides the usual appearances there are described about nineteen atypical forms of the eruption caused by phenolphthalein.[4] It is generally believed that the mechanics of the actual eruption are those of capillary toxicosis. Fatal results have ensued from poisoning by large doses of the drug.[5] In such an instance there was generalized destruction of the endothelial structures with hemorrhages into all the viscera.

REPORT OF CASE

History.—E. K. was an unmarried mechanic 35 years of age. He was admitted to the Jefferson Hospital on Dec. 2, 1933, on account of a cutaneous eruption of seven years' duration and facial neuralgia of several months' standing. The family history was irrelevant. The patient had usually enjoyed good health. An appendectomy had been performed in 1918. There was a history of an acute gonococcic infection four years before examination which lasted three months. No complications or sequels had been noted. There was no history of syphilis. The patient was a steady but "moderate" drinker of whisky. He had not worked for two years on account of his present illness. Gastrointestinal symptoms in recent years consisted of mild attacks of abdominal fulness attributed by the patient to constipation. He had always been more or less troubled in this respect. There were no respiratory or genito-urinary symptoms. He had not had a cutaneous disease, urticaria, asthma or hay fever previously.

Seven years before admission to the hospital the patient began to take a proprietary laxative pill. He had taken two or three at bedtime about twice a week ever since. Each pill contained an uncertain amount of phenolphthalein, and this is said to be the only active ingredient.

---

2. Abramowitz, E. W.: Erythema Multiforme Associated with Cutaneous Pigmentation (Melanin), J. Cutan. Dis. **36**:11 (Jan.) 1918.

3. Newman, B. A.: Phenolphthalein Intoxication, J. A. M. A. **101**:761 (Sept. 2) 1933.

4. (*a*) Loveman, A. B.: Experimental Aspects of Fixed Eruption Due to Alurate, J. A. M. A. **102**:97 (Jan. 13) 1934. (*b*) Walker, Norman: An Introduction to Dermatology, ed. 9, New York, William Wood & Company, 1932.

5. Cleeves, M.: Poisoning by Exlax Tablets, J. A. M. A. **99**:654 (Aug. 20) 1932. Loveman.[4a]

Shortly after he began taking the laxative the patient noticed the eruption of which he complained on admission. He did not recall the definite relation between the first ingestion of the tablets and the original appearance of the dermatosis, but the events nearly coincided. At the beginning the first subjective symptom was burning in the mouth. During later attacks this changed to a puckering sensation so pronounced that it interfered with eating. A red, itching outbreak first involved the back of his neck, and shortly afterward white, painful areas appeared on the mucous membrane of his mouth. Following treatment by a physician the eruption subsided, but it recurred in cycles at about three month intervals, lasting from four to eight weeks each time and slowly disappearing. Gradually the eruption appeared as rounded areas scattered over the surface of the body, and for the past seven years it had been thus generalized in distribution, intensely itchy and varying in color from a brown through violet to a bright red. The patient stated that he occasionally took magnesium sulphate with the aforementioned medication, and at those times the dermatitis was worse. At the time of admission to the hospital he complained of a burning feeling throughout his abdomen.

In an effort to obtain relief from this outbreak the patient consulted numerous private physicians, three hospitals and one dispensary clinic. He recalled having taken various types of internal medication and used numerous salves. Roentgen rays and other forms of radiation had been employed. In April 1933 a sense of pressure was noted in both maxillae. He consulted a dentist and was advised to have all his upper teeth extracted, on the assumption that the cutaneous disturbance was due to some focus of infection there. This suggestion was carried out, but almost immediately afterward localized pain appeared in the right maxilla and had persisted ever since. During inspiration he had the sensation of air entering the maxillary sinus, and when he sneezed a sharp pain occurred in his right cheek, radiating to his right eye and temple. Severe maxillary sinusitis ensued, which caused him to seek aid in the hospital, being referred by his latest physician.

Physical Examination.—The patient was of spare frame and above average height. A cutaneous eruption of general distribution was present, characterized by sharply circumscribed rounded areas varying greatly in size and color. Practically no region was entirely exempt from evidences of the outbreak. Fresh lesions were erythematous and faded on pressure, while older ones consisted only of brownish pigmentation or clusters of freckles. Some areas were lightly desquamating. The lesions varied from 2.5 to 12.5 cm. in diameter. The bearded and mustache regions showed alopecia, presumably from roentgen therapy to patches in those areas.

The upper teeth were absent. At the former location of the first molar in the upper jaw on the right side an opening communicating with the right maxillary sinus was noted. The mucous membrane surrounding this fistula was whitish and tender to pressure. The tonsils were embedded and infected. The cervical lymph nodes were enlarged. Other organs and systems of the body appeared normal on gross examination. Roentgen studies showed evidence of maxillary sinusitis on the right side. On admission to the hospital the hemoglobin content was 95 per cent, the red blood cell count was 5,070,000, the color index was 0.88, and the white blood cell count was 8,500, with a differential count of 68 per cent neutrophils, 2 per cent eosinophils and 28 per cent lymphocytes. The Wassermann and Kahn reactions of the blood were negative. The urine was normal during the patient's stay in the hospital.

Treatment and Course.—The sinusitis was effectively treated. A radical operation on the maxillary sinus, performed on December 14, was followed after an interval by plastic closure of the antral sinus into the mouth. These operations were performed by Dr. C. C. Fox of Prof. Fielding O. Lewis' staff. To control the neuralgia it was found necessary to inject alcohol into the right trifacial nerve. This procedure yielded the desired effect.

The diagnosis of dermatitis medicamentosa from phenolphthalein had been made on admission to the hospital, and the outbreak slowly disappeared after a few days in the hospital without ingestion of the drug. When only pigmented areas were discernible the patient was given 1 grain (0.065 Gm.) of phenolphthalein by mouth. Within five hours generalized pruritus began, and in twelve hours each of the old patches was slightly reddened, especially at the periphery, and itched intensely. During the course of the next twenty-four hours a typical phenolphthalein eruption was present. This decidedly confirmed the diagnosis.

The eruption was quite typical. Practically every part of the body was involved to some extent. The onset was that of generalized pruritus as described

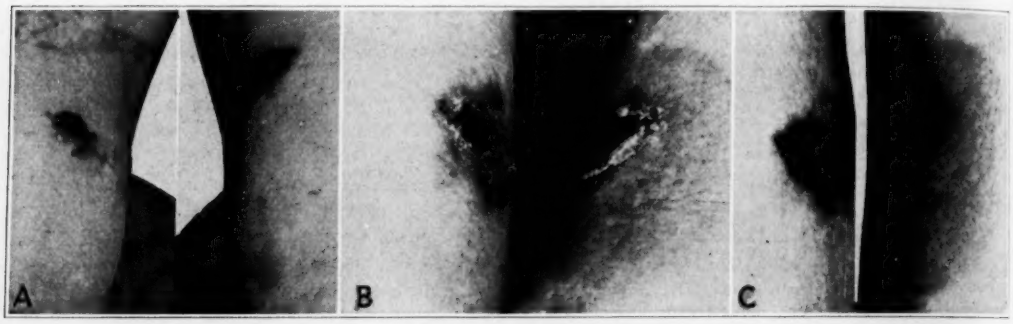

Fig. 1.—A graft of normal skin was moved to the center of an affected patch on the left thigh, and the corresponding piece of affected skin was moved to a normal area on the right thigh. *A* shows the healed grafts on March 20; *B*, both grafts on March 22, sloughing after the administration of ½ grain of phenolphthalein by mouth, and *C*, the grafts on June 4, after the administration of 1 grain of phenolphthalein, with scar tissue in which no change could be noted, although the patch above the left knee showed the usual reaction.

by Walker.[4b] The subjective symptoms were marked, especially the puckering sensation in the mouth. There was also a metallic taste, and the pain in the face was much worse during the outbreak. The larger lesions were definitely sensitive on slight pressure. Older lesions became deep brownish purple. As the color began to subside, some of them exhibited shallow bullae containing a small amount of serum. Nikolsky's sign could be elicited. The roofs of these lesions later became opaque white and ruptured, whereupon the areas desquamated for several days. This was especially noticeable when the areas were subject to trauma, as on the hands and knees. During the height of the outbreak the mucosa of the rectum and sigmoid was observed by sigmoidoscopic examination to be reddened and inflamed. Nearly the entire penis was involved by the eruption.

On Feb. 1, 1934, the patient was given 1/10 grain (6.5 mg.) of phenolphthalein by mouth, which caused only mild subjective symptoms of the same nature and a dusky redness of the lesions after twelve hours.

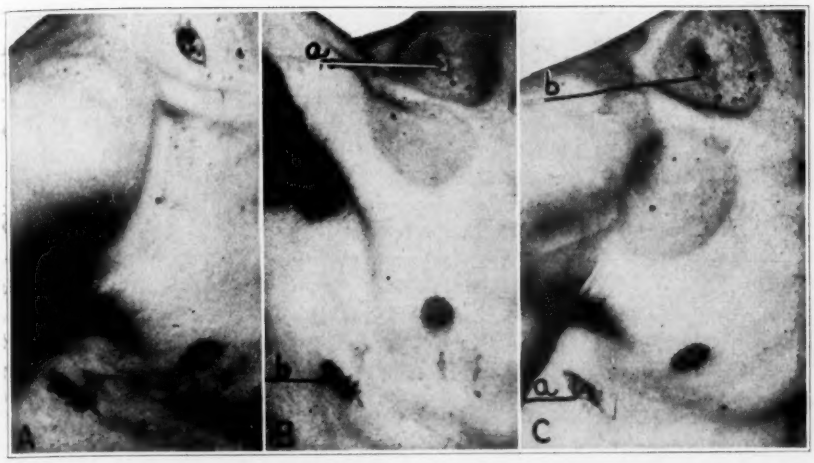

Fig. 2.—A graft of normal skin was moved to an affected patch on the right side of the neck, and the corresponding piece of affected skin was moved to a normal area on the chest. *A* shows the healed grafts on March 20; *B*, both grafts on March 22, after the administration of ½ grain of phenolphthalein, with the graft of normal skin (*a*) showing no reaction and the graft of affected skin (*b*) showing a reaction, although the normal skin surrounding it showed no reaction, and *C*, both grafts on June 4, after the administration of 1 grain of phenolphthalein, with the transplant of previously normal skin to an affected patch on the neck (*b*) seeming to react slightly and the graft on the chest taken originally from the center of a lesion (*a*) showing no reaction.

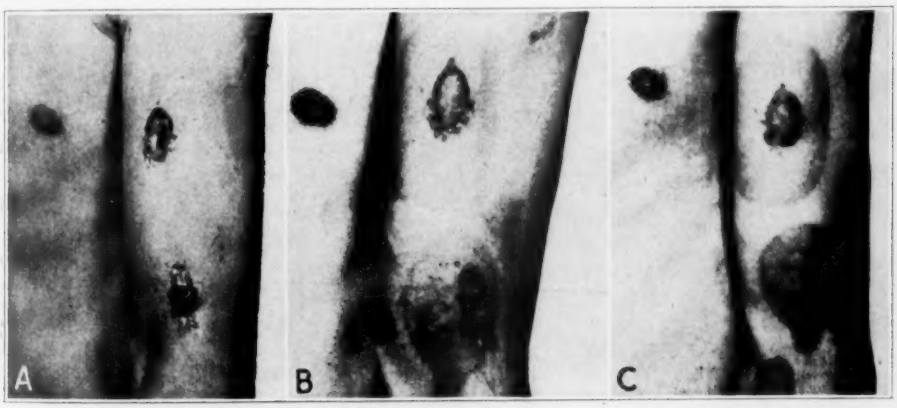

Fig. 3.—On the left arm the centers of two affected patches were interchanged. *A* shows the healed grafts on March 20; *B*, the reaction of both grafts as well as of the surrounding patches on March 22, after the administration of ½ grain of phenolphthalein, and *C*, the reaction of both grafts as well as of the surrounding patches on June 4, following the administration of 1 grain of phenolphthalein.

An attempt was made to study the local cutaneous reaction by the interchange of full thickness skin transplants from the center of affected patches with those from normal skin. This operation was performed in two separate areas, and in a third the centers of two patches were interchanged. The surgical procedure was carried out by Dr. Adolph A. Walkling on February 12. All the grafts healed perfectly. After these transplants were allowed to unite firmly, on March 20 the patient was given ½ grain (0.032 Gm.) of phenolphthalein by mouth. Reacting strongly, two of the grafts which had apparently healed sloughed out, leaving ulcers. These were on the inner aspect of each thigh above the knee and were, respectively, a graft of normal skin moved to the center of an affected patch on the left thigh and the corresponding piece of affected skin moved to a normal area on the right thigh (fig. 1). An affected patch on the right side of the neck into the center of which a piece of normal skin had been grafted reacted strongly, but the transplant of normal skin did not redden (fig. 2 *A* and *B*). There was reaction by the affected skin which had been transplanted to the chest at the point where the normal skin had been obtained, but the surrounding normal skin did not react. On the left arm the centers of two affected patches had been interchanged, and both grafts reacted as well as the surrounding patches (fig. 3 *A* and *B*). The outbreak disappeared sooner than did that produced by the administration of 1 grain of the drug.

Approximately two months later the eruption was again induced by the administration of 1 grain of phenolphthalein by mouth with the following results: The ulcers on the thighs had healed, leaving areas of scar tissue in which no change could be noted, although the patch above the left knee reacted as usual (fig. 1 *C*). The grafts on the left arm reacted with the surrounding areas. The transplant of previously normal skin in an affected patch on the neck seemed to react slightly. The graft on the chest taken originally from the center of a lesion at this time did not react (fig. 2 *C*).

The patient was given one one hundrdeth and later one tenth of the dose of bromsulphonphthalein usually administered intravenously, neither of which injections caused a cutaneous reaction.

Patch tests were carried out with phenolphthalein, bromsulphonphthalein and phenolsulphonphthalein. There was some itching following a test with phenolphthalein over the area of a previous eruption, but there were no reactions otherwise.

Specimens of bile were obtained during a period when the patient had been free from the outbreak for two months. The eruption was induced as previously mentioned, and bile was again obtained. Patch tests were carried on normal and affected skin with the "normal" bile and the "phenolphthalein" bile. There was slight itching in a test with "phenolphthalein" bile over normal skin; otherwise there was no reaction. On a repetition of these tests there was no reaction.

COMMENT

It is obvious that the dosage exerted a marked influence on this patient. Relatively little difference except in the duration of the symptoms was observed between the results of giving 1 grain and ½ grain of phenolphthalein by mouth. There was but slight reaction to ⅒ grain of the drug. If this were entirely a phenomenon of hypersensitivity,

one would expect a fairly marked reaction even to such a small dose. Judging from the symptoms one might assume that the reaction was of a toxic nature.

Patch tests in cases of eruptions caused by phenolphthalein as carried out by other workers have been almost universally negative,[6] although Loveman obtained positive results with allylisopropyl barbituric acid.[4a] Our tests confirmed this finding, although there seemed to be some cutaneous sensitivity in areas of previous eruptions, as evidenced by itching following the patch test with phenolphthalein.

The experiments with skin grafts were undertaken in an effort to determine the primary site of the pathologic change. In the first group the results of the grafts to the left arm and the neck and chest were identical in that the skin already affected continued to react even though moved to another area, while previously normal skin remained in its original state. The fact that the two areas of affected skin reacted, even after having been transposed, clearly demonstrated that the grafting per se had nothing to do with the reaction. The results were identical with those observed by Naegeli.[7] He concluded from his experiments that the skin was the primary site of the process. On the other hand, Wise and Sulzberger [6b] and Loveman [4a] obtained diametrically opposite results and expressed the opinion that the cutaneous manifestation was secondary to some other change. Our observations first agreed with those of Naegeli when the recent transplants were subjected to the effect of the drug, and two months later were in accord with those of the other writers. It is possible to correlate these two findings by the supposition that the transplanted tissues underwent an alteration and later exchanged their natural characteristics for those of their new environment. The result of having the grafts slough had not been observed before. We have no adequate explanation of this, although it is possible that the friction and irritation to which in their situation they were subjected may have been a factor. This was apparently hastened by the inflammation induced by the toxic action of phenolphthalein in the one case in the graft itself and in the other in the surrounding skin.

No previous workers have apparently had the opportunity of repeating the observations after an appreciable length of time. According to our results with the changed reaction of the grafts on the neck and chest (in which a piece of skin which had previously reacted no longer did so after being transposed to a normal area, while previously normal

6. (*a*) Wise, Fred, and Abramowitz, E. W.: Phenolphthalein Eruptions, Arch. Dermat. & Syph. **5**:297 (March) 1922. (*b*) Wise, Fred, and Sulzberger, M. B.: Drug Eruptions, ibid. **27**:549 (April) 1933.

7. Naegeli, O.; de Quervain, F., and Stadler, W.: Nachweis des cellularen Sitzes der Allergie beim fixen Antipyrin Exanthem, Klin. Wchnschr. **9**:924 (May 17) 1930.

skin began to react), it would seem that there was some ulterior influence to which the cutaneous changes were secondary. This could be either nervous or circulatory. As noted earlier, the fundamental pathologic change is probably capillary toxicosis, but the mechanisms of the characteristic localization and fixation of these lesions are as yet unknown. It has been fairly definitely established that the exciting agent of this condition is a split product of the phthalein radical.[3]

SUMMARY

The eruption caused by phenolphthalein is characteristic and sufficiently common to warrant ready diagnosis. A case has been reported illustrating the far-reaching results of failure to recognize this rash.

It is suggested that the mechanism may be predominantly of a toxic nature rather than due to hypersensitivity.

Skin grafts were made from normal skin to affected areas and vice versa and were tested by causing an outbreak. The experiments were repeated after two months. The first results were identical with those of one previous observer and opposite to those of two others. There was a reversal in the results after an interval. It would seem that while there are definite and marked changes in the skin itself, the fundamental pathologic process involved is nervous or vascular.

It was thought that passage through the portal circulation might furnish the toxic factor in the metabolism of the phenolphthalein. While there is some clinical support of this hypothesis, the experiments conducted did not substantiate the theory.

2035 Spruce Street.
527 Penn Street.
Cooper Hospital.

ABSTRACT OF DISCUSSION

Dr. C. Guy Lane, Boston: I think that a word of caution needs to be uttered in regard to testing patients with the drug in view of an instance which occurred at the Massachusetts General Hospital several years ago, when 1 grain of phenolphthalein was given instead of ½ grain. The resulting reaction was intense, with general malaise, pruritus and a burning sensation which required two or three doses of morphine for relief. Since then I have made it a rule to test with ¼ or ½ grain of the drug.

I wish to record a case similar to that recorded by Dr. Abramowitz in which the eruption was the result of the ingestion of frosting on cup-cakes. I talked over this with a candy chemist, and he stated that it is the habit of some manufacturers to pass on to the consumer the recent advances in medicine, in this case, the incorporation of phenolphthalein in sugar.

Dr. E. W. Abramowitz, New York: The paper of Dr. Knowles and his associates was of keen interest to me. I might say incidentally that a study of the literature shows that fixed eruptions may occur from quite a few drugs. In addition to the drugs mentioned by Dr. Knowles, there are reports of reaction following the use of various arsenicals (arsphenamines, acetylarsen and tryparsa-

mide), bismuth isacen, lipoidine-ciba, mercury, quinine, scammonium, sodium salicylate, acriflavine hydrochloride, alcoholic beverages and even after a severe psychic disturbance.

The first autotransplant experiment was reported by Naegeli in 1930. He used the Thiersch graft in transplanting the affected skin to a normal area and the normal skin to the affected spot in a case of a fixed eruption caused by antipyrine. At the end of three weeks, when the graft had healed, Naegeli noted a recurrence in the affected transplanted skin and not in the normal transplanted skin when the patient was given antipyrine. The next experiment was reported by Urbach a few months later, in a case of a fixed eruption caused by phenolphthalein with Naegeli's technic. Urbach also observed a flare-up following the ingestion of phenolphthalein only in the affected transplanted skin, ten days after this graft had healed. Following this Wise and Sulzberger repeated the experiment. However, they used a full thickness skin graft in a patient with a fixed phenolphthalein eruption, and about six weeks later obtained a result opposite to that of the previous investigators; i. e., the normal skin grafted on the affected site flared up instead of the affected skin on the normal site, with the administration of phenolphthalein. Loveman the following year also carried out a full thickness graft (with a biopsy skin punch) in a case of a fixed eruption due to allylisopropyl barbituric acid with results similar to those of Wise and Sulzberger. The drug was administered four weeks and again seven weeks following the grafting.

I hesitate to interpret Dr. Knowles' experiments in view of the apparent equally conflicting results obtained both by himself and also by the aforementioned investigators.

Various methods have been used in an attempt to show that drug eruptions are due to an idiosyncrasy based on allergic sensitization. Cutaneous tests usually give negative results. Experiments in passive transfer except in occasional instances also give negative results. Nevertheless the facts that such eruptions occur in many instances after the patient has been taking the drug previously without any ill effects, that the lesions are not due to cumulative action, that the reaction varies from the normal or pharmacologic effect, that the reaction is specific for that particular drug and that evidently desensitization sometimes occurs, seem to indicate that drug eruptions are of an allergic nature, even though no true antigen-antibody reaction can be demonstrated. Drugs are also capable of causing attacks of hay fever or asthma in those subject to such an affliction. The size of the dose necessary to cause a cutaneous reaction, while small, is variable. I have seen a patient subject to an eruption caused by phenolphthalein in whom a recurrence developed after $\frac{1}{10}$ grain (6.4 mg.) of phenolphthalein was administered. I reported an instance in which iced cup-cakes containing an undetermined but infinitestimal amount of the drug produced a recurrence of the lesions, naturally not as severe as when a larger dose was given. For these reasons I do not agree with Dr. Knowles that the eruptions caused by phenolphthalein are due to the toxic action of the drug.

His experiments with transplants and others of the same type indicate some biologic change that takes place in the affected skin or subjacent structures. In a strict sense this is not a toxic effect, because such changes are neither permanent nor destructive as far as can be demonstrated anatomically. Toxic symptoms occur in almost every one when a poisonous agent is used. On the contrary, a drug eruption occurs only in an occasional person.

The members may recall that at last year's meeting, the question was raised whether phenolphthalein had any toxic effect on the liver. No reports can be found

in the literature except of reactions produced by the halogen salts of phenolphthalein. As soon as the phenolphthalein is combined with the halogens it seems to lose its laxative effect and assumes other qualities. Phenolsulphonphthalein apparently has caused no definitely proved reactions.

It is not plausible to believe that a drug like phenolphthalein that can be taken sometimes in enormous doses even by children without any apparent ill effects should have its action considered toxic when in a small dose it may cause cutaneous eruptions and possibly other general manifestations in an occasional person, especially when such a person took the drug previously with impunity.

Dr. J. Gardner Hopkins, New York: I wish to bring up a point which is largely a matter of terminology, namely, whether these eruptions are toxic or allergic. There are three phenomena that one thinks of as being allergic: The effect is produced in only a small number of persons; the reaction to the drug does not occur until after it has been taken several times with no such effect; the reaction bears no similarity to the known pharmacologic effects of the drug in normal persons.

Dr. Richard S. Weiss, St. Louis: Trauma frequently localizes cutaneous eruptions. It has occurred to me that perhaps trauma may play a part in the production of these fixed eruptions caused by phenolphthalein and I should like to ask Dr. Knowles if he has done any experimental work along these lines.

Dr. Marion B. Sulzberger, New York: I was very pleased to hear Dr. Knowles' excellent paper. I know from experience how difficult it is to do such work. I once said that a patient who would permit these tedious and disagreeable experiments must be an idiot, a fanatic or a physician, or perhaps a combination of all three.

It seems to me that the matter does not stand two to two so far as the skin grafting is concerned. On the contrary, I think that Dr. Knowles has cleared up the cause for the apparent divergence in results. From his experiment it seems that if affected skin is transplanted it carries some of its reactive power with it and reacts no matter where placed. However, if this previously sensitive transplanted skin is allowed to remain for a sufficient time on a previously normal area, it loses its hypersensitivity and becomes normal; and vice versa, normal skin transplanted to a previously affected area eventually becomes hypersensitive.

Dr. Knowles' painstaking and careful experiments have shown that the conception Dr. Wise and I have expressed is probably correct; namely, some underlying lower factor determines the hypersensitiveness of the overlying cutaneous area.

Dr. George Miller MacKee, New York: One difficulty I have encountered is fluctuating sensitivity. There is not always a reaction in cases of fixed eruption when the drug is given as a test.

Dr. Frank C. Knowles, Philadelphia: The study we made has been extremely interesting. My colleagues and I were able to keep the patient hospitalized for several weeks at a time on several different occasions. The work was carried out in detail, with very minute doses, fair doses and large doses, to see what the effect would be. We tested with bile and with bile taken after the drug had been given, which must have contained a certain amount of phenolphthalein, and used all the experiments we could to see whether positive patch tests would result by application of the drug. The patch tests with phenolphthalein did not cause positive reaction, but some pruritus of the skin was produced.

When we referred in the paper to fixed eruption due to certain drugs, we meant those drugs which characteristically cause this type of eruption. We have found the fixed type to be caused by just four drugs.

Along the line of Dr. Abramowitz's comments I wish to state that our results were just the same as those of Naegeli in the beginning and as those of Wise and Sulzberger later.

One fact Dr. Sulzberger mentioned that I think is extremely interesting is that his and Dr. Wise's results were obtained some months after the skin grafting was carried out. Our results were obtained approximately five weeks after a full thickness skin graft had been transplanted and corresponded to those reported by Naegeli; two months later, however, on administration of the drug, the grafts exhibited the same results as those recorded by Dr. Wise and Dr. Sulzberger, showing that the skin had returned to a normal condition and reacted differently than it did in our first experiment.

EXTENSIVE PIGMENTED NEVUS ASSOCIATED WITH PRIMARY MELANOBLASTOSIS OF LEPTOMENINGES OF BRAIN AND SPINAL CORD

REPORT OF A CASE

E. W. NETHERTON, M.D.
CLEVELAND

The study of the nature and origin of nevi, their harmful potentialities and their relation to associated congenital malformations of other ectodermal structures presents many interesting and complex problems. During the last decade, fairly well established concepts concerning the nature and origin of nevi have been altered or discarded by several competent investigators, and the apparent significance of the association of certain groups of neurologic signs and symptoms with nevoid changes in the skin has resulted in the recognition of the neurocutaneous syndromes.

Dermatologists have long been familiar with the occasional association of neurofibromatosis and lowered mentality and with the association of adenoma sebaceum and epilepsy and feeblemindedness; however, the neurologist and the neurosurgeon, for obvious reasons, have led the way in the correlation of associated neurologic findings and cutaneous congenital malformations.

It is reasonable to suspect that melanotic congenital malformations may occur in the meninges of the central nervous system either independently or in association with pigmented nevi of the skin. It seems possible that aberrations in the development of the ectodermal layer may result in congenital malformations of the central nervous system other than those observed in cases of the recognized neurocutaneous syndromes. The most common melanotic tumor of the central nervous system is metastatic in origin; however, cases of primary melanoma of the meninges have been reported. In rare cases, extensive pigmented nevi of the skin were apparently associated with independent melanoblastosis of the meninges. Recent studies of the embryologic development of the meninges as well as advancements in the knowledge of the histogenesis of nevi lend support to the suggestion that melanotic congenital anomalies may occur in the meninges. It being realized that

Read at the Fifty-Eighth Annual Meeting of the American Dermatological Association, Inc., White Sulphur Springs, W. Va., May 4, 1935.

such a concept is contrary to the orthodox beliefs, the following case is reported:

REPORT OF CASE

History.—A youth, aged 17, first came to the Cleveland Clinic on Sept. 2, 1931. He had been well until seven weeks prior to his admission, when he began to have frontal and occipital headaches, which gradually increased in severity. The headaches were accompanied by progressive blurring of vision and loss of memory. During the four weeks prior to examination there had been almost daily projectile vomiting. The patient was continually drowsy but slept poorly. The right hand felt numb at times. There was hesitancy on urination. Sharp pains had been present in both legs and thighs, and he had suffered from generalized pruritus for several days. No history of trauma was elicited.

Neither the past nor the family history was significant.

Physical Examination.—The patient was fairly well nourished, although he was of the asthenic type. With the exception of the cutaneous and neurologic signs, there were no abnormalities of significance.

A large hairy nevus was present over the lateral surfaces of the face, neck and scalp, both the anterior and the posterior portion of the trunk and the arms. Scattered over the entire body were many smaller nevi, varying from 1 to 5 cm. in diameter. They were of the same color as the large lesion, and they also were covered with coarse black hair. These lesions had been present since birth. Papulovesicular and excoriated lesions were distributed over the trunk, chiefly in the axillary folds and on the abdomen. This eruption was present on the penis, the buttocks, the wrists and the webs of the fingers. The extensive distribution of the deeply pigmented nevus obscured the characteristics of the eruption.

There were no indications of a localized neurologic lesion. The pupils were somewhat enlarged, but they reacted normally. The disks showed 4 or 5 diopters of edema, and there was definite concentric contraction of both visual fields. Numerous hemorrhages were observed in the right eye. All the deep reflexes were sluggish, but no pathologic reflexes were elicited.

Clinical Diagnosis.—The following diagnosis was made: increased intracranial pressure, probably resulting from tumor of the brain; pigmented hairy nevus, and scabies.

Further Examination.—The following studies and observations were made: A roentgenogram of the skull and sella turcica revealed no abnormality. The patient was admitted to the hospital, and a spinal puncture was performed. With the patient in the horizontal position, the spinal fluid pressure measured considerably over 700 mm. of water. The following day an encephalogram was made. One hundred and ninety cubic centimeters of fluid was gradually replaced with 189 cc. of air. The spinal fluid was slightly yellow. Films taken at this time revealed absence of air in the subarachnoid space and moderate dilatation of the ventricular system. The fourth ventricle was poorly visualized. From these findings a diagnosis of probable cerebellar tumor was made. Examination of the spinal fluid revealed 17 lymphocytes, a trace of globulin and a total protein content of 45 mg. per hundred cubic centimeters. The Wassermann and the colloidal gold chloride test gave negative results. The Wassermann reaction of the blood was also negative.

Observations at Operation.—Suboccipital craniectomy was performed, which revealed a normal cerebellum without herniation. The posterior surface of the

medulla was covered with a bluish-gray mantle, suggesting a venous angioma. Dr. W. J. Gardner was unable to determine how far the lesion extended down the cord. Exploration of the inferior surface of the cerebellum, both cerebellopontile angles and the fourth ventricle revealed nothing abnormal. A postoperative diagnosis of venous hemangioma of the medulla was made; however, this did not satisfactorily explain the increased intracranial pressure, because the lesion was not obstructing the ventricles.

Postoperative Course.—The patient had a stormy postoperative course and was irrational for several days. Eight days after operation, high voltage roentgen therapy was started. On the tenth postoperative day, he was more rational and showed improvement, but he still had slight headache. Antiscabetic therapy had not relieved the pruritus. The patient left the hospital on the seventeenth postoperative day, and at this time the spinal fluid pressure measured 180 mm. of water. The fluid was yellow and contained 11 cells; the reaction for globulin was four plus, and the total protein content was 975 mg. per hundred cubic centimeters.

The patient returned one month later. He had been well until three days before, when the severe headaches, vomiting and nervousness recurred. There was bulging in the area of the previous craniectomy wound. The visual fields were grossly normal, but the disks revealed about 4 diopters of edema. The generalized pruritus had become worse.

Three days after the second admission to the hospital, spinal puncture was performed with the patient under tri-brom-ethanol in amylene hydrate anesthesia. The spinal fluid pressure was 580 mm. of water, and no pulsations were noted in the manometer. The fluid was yellow and soon coagulated on standing. The cell count was high, most of the cells being red corpuscles; the reaction for globulin was four plus, and the total protein content was 3,250 mg. per hundred cubic centimeters.

Twenty-two cubic centimeters of fluid was removed and 20 cc. of air injected, but the air was returned. Although clinical signs or symptoms of tumor of the spinal cord were not exhibited, the findings indicated a subarachnoid block fairly low in the spinal canal. Therefore, the right ventricle was tapped through the preexisting trephine opening, and 75 cc. of clear, colorless fluid was removed. The fluid contained 60 cells per cubic centimeter, and the total amount of protein was 60 mg. per hundred cubic centimeters. One and five-tenths cubic centimeters of iodized poppy-seed oil 40 per cent was injected into the ventricle, and the head was manipulated in an effort to allow the oil to run down the spinal canal. Roentgenograms taken at intervals during the next five days showed oil as low as the seventh and eighth dorsal vertebrae.

Observations at Second Operation.—Since the condition of the patient did not improve, cervical laminectomy was performed one week after his admission to the hospital. The spinous processes and laminae of the second, third and fourth cervical vertebrae were removed, and a large collection of subarachnoid fluid was evacuated from the cisterna magna. The spinal cord throughout the extent of the exposure was completely obscured by the bluish-gray mass which was seen at the first operation but which appeared to be larger at the time of the second. In the lower portion of the exposure, the mass completely occluded the lumen of the vertebral canal. It was thought that the return of symptoms was the result of adhesions which had formed about the foramen of Magendie. Therefore, these adhesions were separated and the fourth ventricle was opened, but there were no lesions in the ventricle. Since the condition was inoperable, the wound was closed without drainage.

Course.—The patient became irrational and stuporous and died two days after operation. We were unable to explain the severe itching which was present throughout the period of observation.

Macroscopic Observations at Autopsy.—A partial autopsy was permitted, and the brain and spinal cord were removed. The brain, including the dura and the first four or five segments of the spinal cord, weighed 1,565 Gm. after fixation in formaldehyde. There were no tumors of the dura, and the sinuses of the dura appeared to be normal. The vessels of the pia were markedly injected over the entire superior and lateral surfaces of the cerebrum. The pia-arachnoid over the base of the brain was slightly thickened and brownish. From the optic chiasm to the pons, the medulla and the upper portion of the cervical region of the cord, the pia-arachnoid was considerably thickened. Multiple sections through the cerebrum showed moderate, uniform dilatation of the lateral ventricles. The third

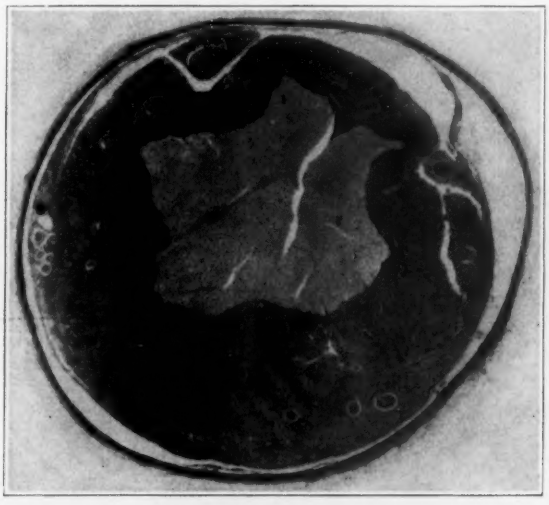

Fig. 1.—Cross-section of the lower dorsal portion of the spinal cord, showing the sheath of neoplastic tissue limited to the pia-arachnoid.

and fourth ventricles and the aqueduct were little dilated. Except congestion of the vessels, there were no gross lesions within the cerebrum, pons, medulla and cerebellum.

The dura of the cord was normal. A sheath of tumor tissue occupied the site of the pia-arachnoid, which completely surrounded the cord from the level of the medulla to the cauda equina (fig. 1). The tumor tissue was uniform, cellular and grayish brown, and it completely filled the space between the cord and the dura. It varied in thickness from 1 to 5 mm. at various levels of the cord. The greatest thickness was in the midcervical and lumbar regions. The dura stripped from the tumor sheath without difficulty, and it was not infiltrated at any point. The tumor tissue surrounded the spinal nerves as they emerged from the cord. The nerve trunks of the cauda equina were also surrounded by tumor tissue (fig. 2). The cord was somewhat distorted, irregular and diminished in size, but there was no invasion of the cord by the tumor.

Histologic Observations.—Histologic study was made of tissue from the cerebral and cerebellar cortex, pons, medulla oblongata, spinal cord, cauda equina, olfactory nerve and choroid plexus and from the nevus of the scalp. Since the material was fixed in formaldehyde, I was unable to use Masson's technic of staining, which is essential if one is to demonstrate the close relationship of the nevus cells to the nerve tissue. As a substitute, silver-impregnated sections were prepared by the method advised by Foot and Zeek,[1] but they were unsatisfactory

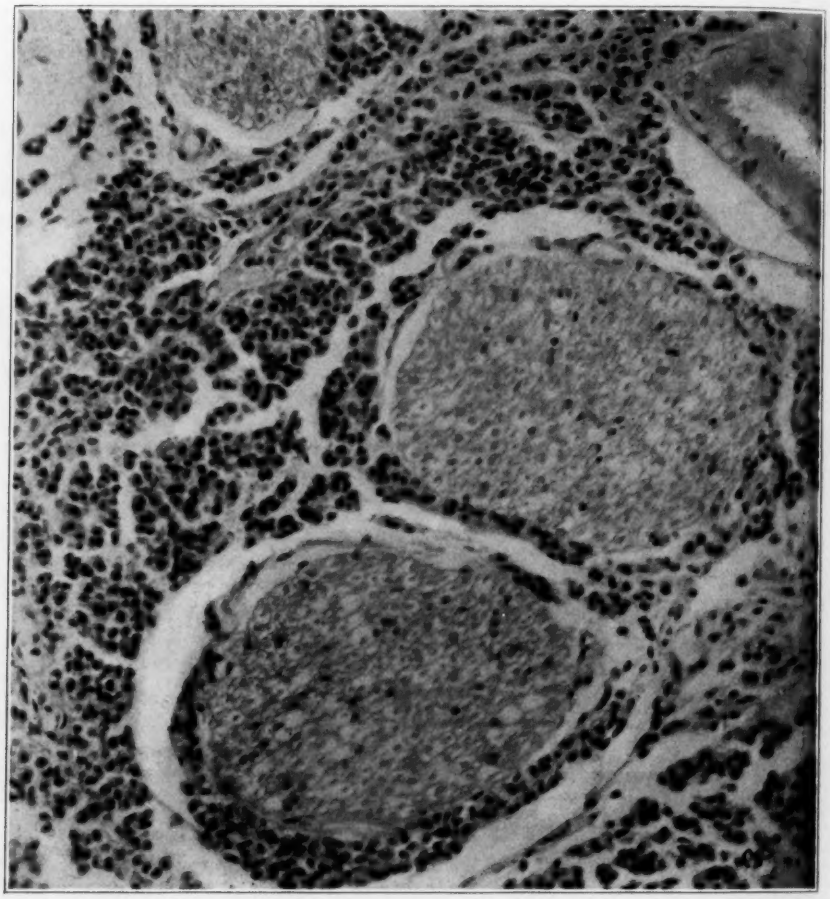

Fig. 2.—Section (× 200) of the cauda equina with dense cellular infiltration surrounding the nerve bundles. The nerves are not involved.

for the study of nerve structures. The preparation as well as the interpretation of sections impregnated with silver necessitates special skill and experience; otherwise, observations and conclusions are worthless. Consequently, my observations are limited mainly to the study of sections stained with hemotoxylin and eosin.

1. Foot, N. C., and Zeek, P.: Two Cases of Melanoma of Meninges with Autopsy, Am. J. Path. **7**:605 (Nov.) 1931.

Fig. 3.—Section of the superficial portion of the nevus (× 200).

Epidermis: The epidermis over the nevus was thin, and the papillary bodies had been obliterated. There was a moderate amount of hyperkeratosis, and the granular layer consisted of one or two layers of cells. The rete mucosum was thin, and in some areas the cells were poorly stained and had elongated or distorted nuclei; however, in most areas the rete mucosum was normal. The basal layer was intact, but its pigment content varied considerably in different areas. The epidermis did not contain groups of nevoid cells, and there were no apparent connections between the epidermis and the nevus cells in the corium.

Corium: In the superficial portion of the corium was a zone of connective tissue in which the cells were comparatively few. This zone separated the epidermis from the complex or polymorphous nevoid cellular infiltrate which involved the corium and extended into the hypoderm.

The more superficial portion of the nevus consisted of cells with a small amount of protoplasm and large round or oval vesicular nuclei, poor in chromatin (fig. 3). The cells were arranged in clusters and cords, which were separated by strands of collagenous connective tissue. The cell nests, which were well circumscribed, had a fine reticulum. Scattered throughout this portion of the nevus were large multinucleated cells or giant nevus cells. Large irregular cells containing coarsely granular brownish pigment were scattered throughout the superficial portion of the nevus. In the deeper portions of the corium, the connective tissue stroma was more abundant, and the nuclei of the nevus cells, which were smaller than those in the superficial layers, were more deeply stained. The cellular infiltration was not so dense; the cells appeared individually or as strands, which mostly were parallel with the epidermis.

In the lower portion of the corium and extending into the subcutaneous tissue, there were large and small, well circumscribed, interlacing and incompletely anastomosed cellular bundles or funiculi (fig. 4). The areas were composed of large round or polygonal cells with poorly stained cytoplasm and round or oval well stained nuclei. The cells in the central portion of the funiculi contained a large amount of protoplasm, and their nuclei were large, round and fairly rich in chromatin, while at the periphery the amount of cellular protoplasm was decreased and the nuclei were smaller, spindle-shaped or oval and rich in chromatin. No pigment-containing cells were seen in the deep portion of the nevus.

There were numerous blood vessels throughout the nevus, but no intimate relationship existed between the nevus cells and the vascular endothelium. There was no endothelial proliferation.

Hair follicles and sebaceous glands appeared sparsely throughout the nevus and were completely separated from it by a zone of connective tissue. The nevus was free from mitotic figures, and there were no areas of alveolar arrangement of the cells commonly seen in malignant melanomas. The structure was similar to that of the giant neuronevus of the scalp which was described by Masson.[2]

Sections of the cerebral cortex, olfactory bulb, pons, thalamic region and medulla oblongata showed no noteworthy histologic abnormalities of the substance of the brain. However, there was a diffuse growth of undifferentiated cells involving the pia-arachnoid in all the sections. Small areas of tumor cells were present in sections of the choroid of the lateral ventricles. The tumor cells had relatively large round or oval nuclei which contained considerable chromatin. The cell borders were indistinct.

---

2. Masson, P.: Giant Neuro-Naevus of the Hairy Scalp, Ann. Surg. **93**:218 (Jan.) 1931.

The growth consisted of a loosely arranged cellular infiltration of variable thickness, which was limited to the pia-arachnoid. The tumor cells completely surrounded the pial vessels of the sulci and some of the vessels in the deeper portions of the brain, but they did not invade the parenchyma of the brain (fig. 5). Mitotic figures were absent in the sections of the brain and medulla.

Sections at various levels of the spinal cord from the upper portion of the cervical region to and including the cauda equina showed a thick mantle of cells

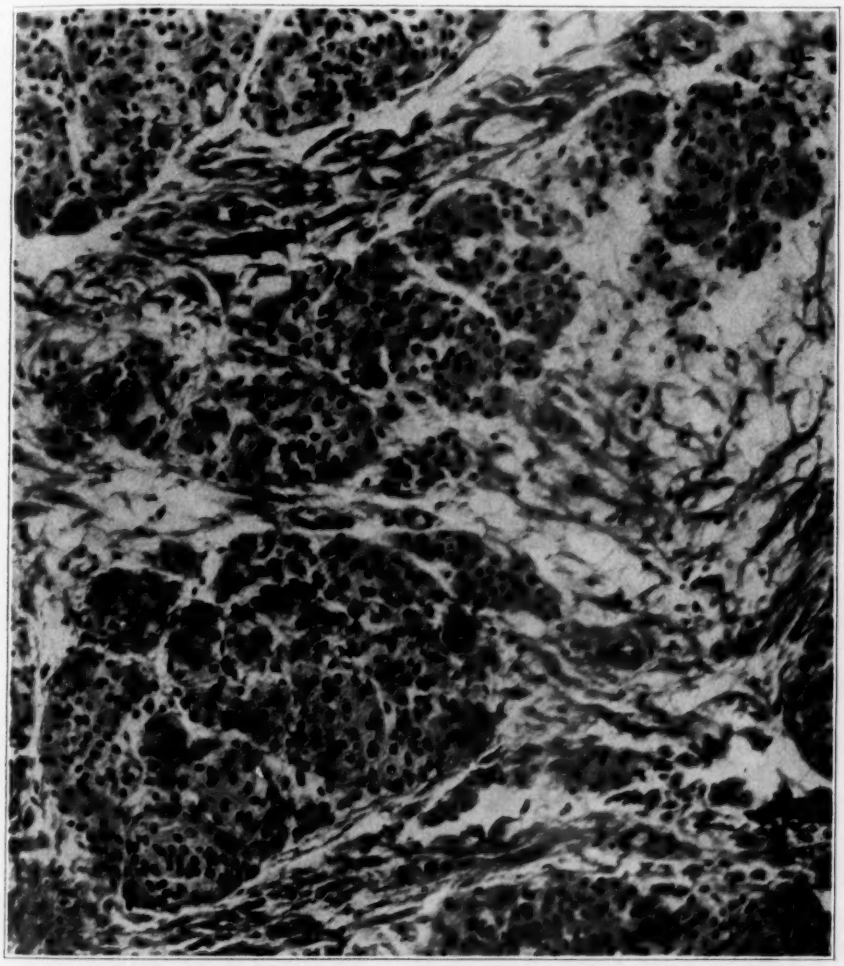

Fig. 4.—Section of the deep portion of the nevus consisting of neuroid bundles forming a fasciculated neurinoma (× 200).

completely surrounding the cord, the nerve trunks of the cord and the individual bundles of the cauda equina. The cellular cloak, which varied in thickness at different levels of the cord, was confined to the leptomeninges and did not invade the substance of the cord or nerves. The pial vessels penetrating the cord and its commissures, like those observed in the sections of the brain, were surrounded

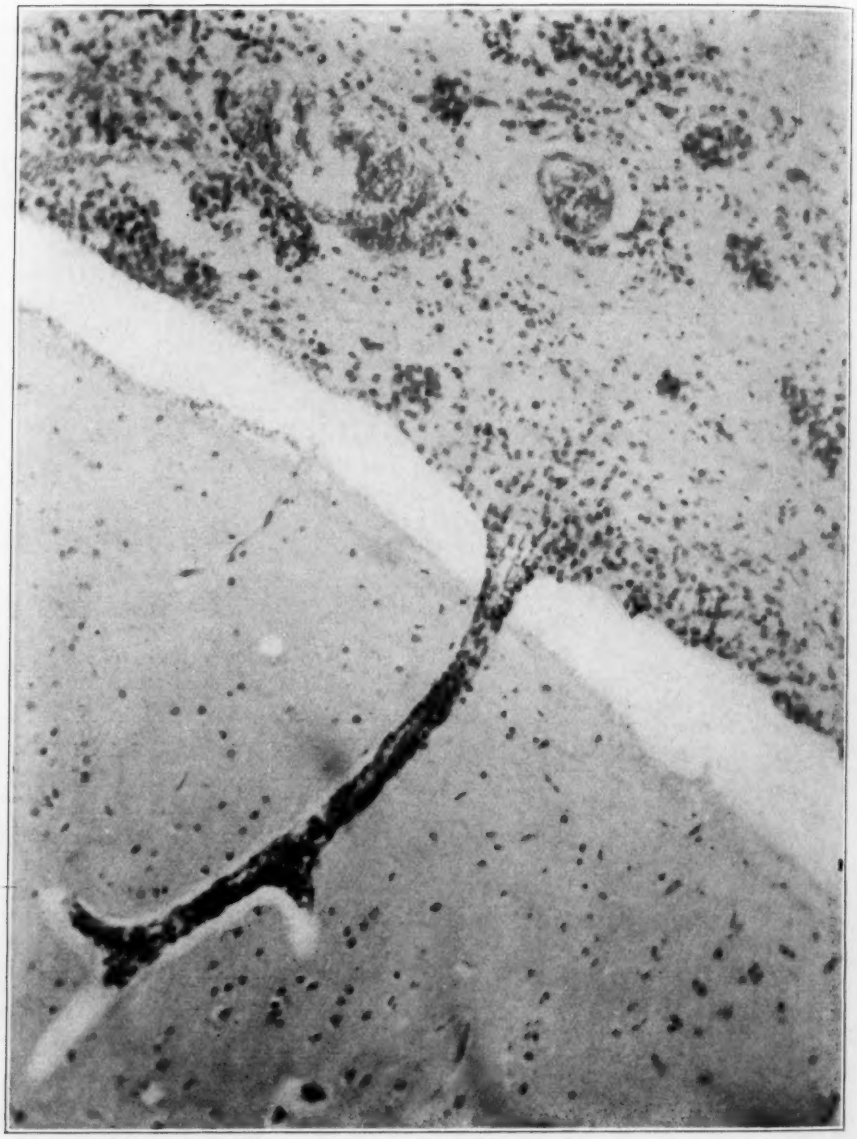

Fig. 5.—Section (× 200) of the cerebral cortex, showing the limitation of tumor tissue to the pia-arachnoid. A pial vessel entering a sulcus of the brain is surrounded by tumor cells; however, the nerve tissue is not invaded by the neoplasm.

by tumor cells. At several levels the spinal cord was compressed and distorted. The changes in the leptomeninges of the cord consisted mainly of a dense infiltration of undifferentiated cells with large oval vesicular nuclei and a variable amount of protoplasm (fig. 6).

The chromatin content of the nuclei of the cells varied considerably. The cells were identical with those observed in the meninges of the brain except that they were larger. In several areas there was an alveolar formation of the cells, and

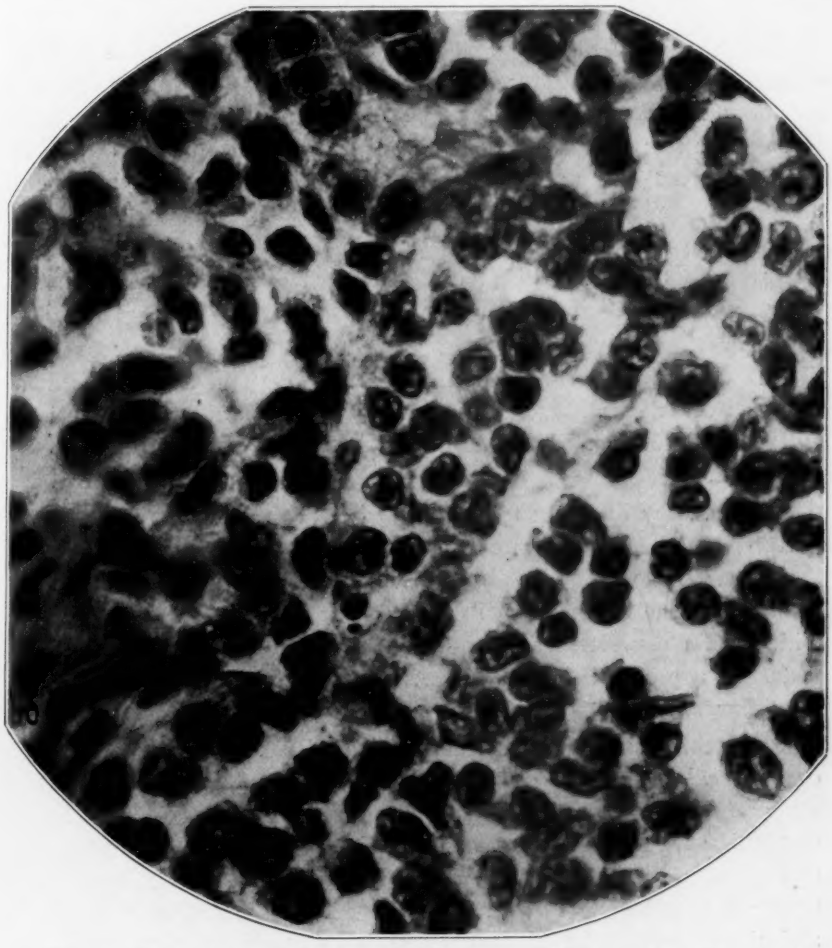

Fig. 6.—Photomicrograph taken with high magnification (× 450), showing the large undifferentiated cells observed in the melanoblastoma of the leptomeninges.

where the cellular proliferation was less marked a definite perithelial arrangement was evident. There was very little connective tissue stroma in the densely infiltrated areas. Mitotic figures were present but were not numerous. Scattered throughout the sections and especially around the blood vessels were numerous irregular cells which contained coarsely granular yellowish-brown pigment. The blood vessels showed no evidence of endothelial proliferation.

Although the neurocutaneous syndrome in this case does not conform entirely to any recognized type, a brief outline of the syndromes and a review of some of the literature concerned with the interpretation in this case are given. In a broader sense, it would seem that a proper approach to this question would be the discussion not only of the recognized neurocutaneous syndromes but of other conditions which may be the result of widespread developmental derangements of the ectoderm.

REVIEW OF THE LITERATURE

Yakovlev and Guthrie [3] were among the first to classify these syndromes. They studied a group of patients with epilepsy whose congenital malformations involved the ectodermal structures, and they endeavored to correlate this relationship with the associated neurologic and psychic manifestations. They applied the term congenital ectodermoses to these symptom complexes or to the neurocutaneous syndromes, which they divided into three main groups: (1) Recklinghausen's neurofibromatosis; (2) Bourneville's tuberous sclerosis, and (3) angiomatosis of the brain, with nevi of the skin in the trigeminal area.

As one would suppose, as a result of the great variation in congenital defects which may occur in the skin and nervous system, the condition in many cases does not conform to any of the three types of neurocutaneous syndrome. This fact has been emphasized by Kulchar and Anderson.[4]

It is not my intention to discuss at length the neurocutaneous syndromes, because Yakovlev and Guthrie [3] and Kulchar and Anderson [4] have done this well. However, a brief description of each type will demonstrate the importance of the evaluation of the association of nevi with certain neurologic or mental symptoms in some cases. In most instances, a proper interpretation of the cutaneous changes will clarify the diagnosis.

In Recklinghausen's disease, the principal lesions are (1) soft, flat or pedunculated tumors of the skin, (2) tumors which develop along the peripheral nerve trunks and occasionally in the central nervous system, usually in the meninges (arachnoid) or in the roots of the cranial and spinal nerves, and (3) pigmented nevi or "café au lait" spots scattered over the body. There may be considerable variation in the triad, and the dermatologist is familiar with this type of neurocutaneous syndrome.

---

3. Yakovlev, P. I., and Guthrie, R. H.: Congenital Ectodermoses (Neurocutaneous Syndromes) in Epileptic Patients, Arch. Neurol. & Psychiat. **26**:1145 (Dec.) 1931.

4. Kulchar, G. V., and Anderson, L. E.: Neurocutaneous Syndromes: Congenital Ectodermoses, Arch. Dermat. & Syph. **30**:211 (Aug.) 1934.

Bourneville's tuberous sclerosis or epiloia was first described by Bourneville and Brissaud in 1880.[5] Of the three neurocutaneous syndromes it is the most clearcut in respect to the clinical and pathologic characteristics, and according to Yakovlev and Guthrie [3] it is the most constant in its association with mental defects and epilepsy. The chief dermatologic manifestation of tuberous sclerosis is the presence of multiple yellowish-pink or brownish-red nodules on the face with a predilection for the nasolabial folds, associated with mental deficiency and epileptic seizures. The cutaneous manifestation is a nevoid condition, known as adenoma sebaceum. Tumors and cysts of the kidneys and other viscera are frequently observed concomitantly.

Adenoma sebaceum is not always the nevoid change that is observed in this type of neurocutaneous syndrome, as is demonstrated in the cases described by Fabing,[6] who was the first to report the occurrence of tuberous sclerosis in monozygotic twins. In his cases the nevoid changes consisted of vascular nevi of the neck, naevus anemicus (of Vorner) and pigmented fibromatous nevi over the second lumbar vertebra. The neurologic signs were weakness of one side of the face and epileptic seizures. The cutaneous lesions were mirror images of the neurologic signs. Fabing suggested that the mirror imaging of the cutaneous and neurologic manifestations is similar to the transposition of viscera occasionally seen in monozygotic twins, and he reasoned that the anlagen of tuberous sclerosis and allied conditions exist very early in the life of the zygote. Like neurofibromatosis, this condition may be hereditary and familial.

The pathologic changes in the central nervous system consist of hard yellowish-white nodules and sclerotic areas of the brain, which show a predilection for the cortex of the frontal lobes. The sclerotic changes are the result of glial hyperplasia.

Angiomatosis of the brain with nevi of the skin in the trigeminal area, the third main type of neurocutaneous syndrome, consists of vascular nevi of trigeminal distribution associated with neurologic signs and symptoms which result from congenital vascular malformations of the central nervous system. Within the last decade the frequency of association of angiomatosis of the brain and that of the skin has been emphasized.

Cushing [7] commented on the frequency with which portwine nevi of the face involved areas of the skin which were innervated by one or

5. Bourneville and Brissaud, cited by Yakovlev and Guthrie.[3]

6. Fabing, Howard: Tuberous Sclerosis with Epilepsy (Epiloia) in Identical Twins, Brain **57**:227 (Dec.) 1934.

7. Cushing, Harvey: Cases of Spontaneous Intracranial Hemorrhage Associated with Trigeminal Nevi, J. A. M. A. **47**:178 (July 21) 1906.

more branches of the trigeminal nerve, and he observed that in exceptional cases the nevus involved the entire area of the skin supplied by the trigeminal nerve. Cushing expressed the belief that the correspondence of the topographic distribution of the nevus with the segmentally innervated fields of the skin suggested that a prenatal lesion occurring in the ganglion or in one of its component parts may have been responsible for the production of the nevus, just as in adult life the trophic changes in zoster are the result of inflammatory reaction in the ganglion. He credited Bärensprung with being the first to study the topographic distribution of nevi and their relation to territories of cutaneous innervation. Cushing suggested that organs other than the skin but innervated by the same nerve segment could be similarly affected. In the case reported by Cobb,[8] the condition is an excellent demonstration of the neuromeric distribution of congenital vascular anomalies which is characteristic of this type of neurocutaneous syndrome. The case was that of a boy 8 years of age who suffered from paraplegia, with the upper level of anesthesia at the tenth thoracic segment. A few small portwine nevi occurred on the areas of the back supplied by the seventh, eighth and ninth dorsal segments. Operation revealed a vascular tumor overlying the cord from the fourth to the ninth dorsal segment.

In 1926 Lindau,[9] while studying cysts of the cerebellum, noted their frequent association with angiomatosis of the retina (Hippel's disease) and occasionally with cysts and tumors of other organs. He concluded that the cerebellar cysts arose from congenital hemangiomas. Two years later Cushing and Bailey [10] showed that venous angiomas of the brain are often associated with vascular nevi of trigeminal distribution. The authors agreed with Lindau in regard to the congenital mesodermal origin of the cerebellar hemangiomas and called the neoplasms hemangioblastomas.

The encephalotrigeminal type of congenital vascular malformation has been reported by a number of authors, among others by Wilson,[11]

---

8. Cobb, S.: Haemangioma of the Spinal Cord Associated with Skin Naevi of the Same Metamere, Ann. Surg. **62**:641 (Dec.) 1915.

9. Lindau, A., cited by Yakovlev and Guthrie.[3]

10. Cushing, H., and Bailey, P.: Tumors Arising from the Blood Vessels of the Brain: Angiomatous Malformations and Hemangioblastomas, Springfield, Ill., Charles C. Thomas, Publisher, 1926, p. 211; Hemangiomas of Cerebellum and Retina (Lindau's Disease) with Report of a Case, Arch. Ophth. **57**:447 (Sept.) 1928.

11. Wilson, A. J.: Cutaneous and Meningeal Haemangiectatic Nevi: A Note on Cutaneous and Meningeal Hemangiectatic Nevi Associated with Contralateral Epilepsy and Hemiplegia (Syndrome Neurocutane), J. Neurol. & Psychopath. **14**: 349 (April) 1934.

Rocke,[12] Ellis,[13] Brushfield and Wyatt,[14] Aynsley,[15] Weber[16] and others.

Since angiomas arise from tissue of mesodermal origin, it is difficult to justify the inclusion of these anomalies in the group of ectodermal dermatoses. Yakovlev and Guthrie[3] expressed the belief that congenital vascular anomalies may have their origin in a developmental defect of the vasomotor (neuro-ectodermal) or the sympathetic innervation and that the blood vessels result from superimposed hyperplasia of mesodermal tissues.

Virchow[17] recorded the first case of melanosarcoma of the arachnoid and attributed its origin to the chromatophores of the leptomeninges. He stated that the pigmented areas, first described by Valentine, which occur in the arachnoid are frequently present in elderly persons of the Caucasian race. They are observed frequently on the anterior surface of the medulla oblongata and the cervical portion of the spinal cord and at times over the base of the brain.

In Virchow's case the patient was a copperplater, aged 30, who had suffered from repeated attacks of painter's colic. He became incompletely paralyzed and almost blind. Autopsy revealed numerous scattered ecchymoses and yellowish-brown pigmented spots on the surface of the right hemisphere. At the base of the brain there was a widespread circumscribed and nodular melanotic deposit in the pia mater. The entire length of the cord was surrounded by the melanotic tissue. The sheaths of the spinal and cranial nerves were also involved, but the growth did not extend beyond the ganglions. The eyes and the rest of the body were normal. In no place did the neoplasm penetrate the substance of the brain or spinal cord. Histologic examination showed infiltration of short spindle cells arranged in fasciculi, while in the areas of greatest proliferation the cells were of the small granulation tissue type.

---

12. Rocke, J. M.: Association of Extensive Hemangiomatous Naevus of Skin with Cerebral (Meningeal) Haemangioma, Proc. Roy. Soc. Med. **25**:793 (April) 1932.

13. Ellis, R. W. B.: Trigeminal Naevus and Hemangioma of Meninges, Proc. Roy. Soc. Med. **25**:1732 (Oct.) 1932.

14. Brushfield, T., and Wyatt, W.: Hemiplegia Associated with Extensive Nevus and Mental Defect (Pathological Changes), Brit. J. Child. Dis. **24**:98 (April-June); 209 (July-Sept.) 1927; **25**:96 (April-June) 1928.

15. Aynsley, T. R.: Hemiplegia Associated with Extensive Nevus and Mental Defect, Brit. J. Child. Dis. **25**:197 (July-Sept.) 1928.

16. Weber, F. Parkes: Notes on Association of Extensive Haemangiomatous Naevus of Skin with Cerebral (Meningeal) Hemangioma, Especially Cases of Facial Vascular Naevus with Contralateral Hemiplegia, Proc. Roy. Soc. Med. **22**:431 (Feb.) 1929.

17. Virchow, R.: Pigment und diffuse Melanose der Arachnoides, Virchows Arch. f. path. Anat. **16**:180, 1859.

Grahl [18] reported a case which in many respects was similar to that reported in this paper. Autopsy performed on the body of a new-born child revealed structures which he was unable to find described in the literature. A giant pigmented or bathing-trunk nevus and numerous smaller pigmented spots scattered over the entire body were associated with symmetrically arranged pigmentation of the cerebrum and cerebellum and malformation of the cerebral cortex. A thorough microscopic examination of all the organs of the body established the fact that the essential abnormal changes were limited to the skin and brain. All the viscera were free from melanotic neoplasms. Grahl concluded that in his case it was demonstrated that a grave malformation of the skin, characterized by an extensive pigmented nevus, may be associated with an apparently independent simultaneous malformation of the central nervous system. He expressed the belief that the pigmented cells of the nervous system originated from neuro-epithelial elements.

Boit [19] found in the literature reports of only seven cases of primary melanotic tumor of the central nervous system. A case of melanoma of the brain was reported by Minelli; two of the spinal cord were described by Pick and Herschberg, and four instances in which the meninges were involved were recorded by Virchow, Sternberg, Stoerck and Thorel, respectively. Boit was the first to observe primary melanoma of the dura mater. Most cases which he reviewed were characterized by tunic-like cloaking of the vessels of the meninges by tumor cells, diffuse involvement of the meninges and absence of metastases to other portions of the body. In most instances of primary melanoma of the meninges, the nerve tissue was not invaded. Boit cited cases described by Grahl, Rokitansky and Oberndorfer in which there were numerous pigmented nevi associated with degeneration of the chromatophore of the pia as instances of systematically arranged developmental disturbances analogous to multiple exostoses and multiple neurofibromas. Boit explained the primary involvement of the dura on the basis of the theory of the bursting of pial chromatophores.

Berblinger [20] reported the case of a girl 9 months of age in whom at birth one hundred and ninety partly hairy pigmented nevi were scattered over the body. Death resulted from congenital hydrocephalus. A thorough postmortem examination revealed a melanotic tumor of the brain, a glioma of the pons, sarcomatosis of the meninges and neuro-

18. Grahl, F.: Angeborener ausgedehnter Naevus pigmentosus in Verbindungen mit Pigmentflecken im Gehirn, Beitr. z. path. Anat. u. z. allg. Path. **39**:66, 1906.

19. Boit, Hans: Ein Fall von Chromatophoroma durae matris spinalis: Beitrag zur Kenntnis des Chromatophoroma piale, Frankfurt. Ztschr. f. Path. **1**:248, 1907.

20. Berblinger, W.: Ein Beitrag zur epithelialen Genese des Melanins, Virchows Arch. f. path. Anat. **219**:328, 1915.

fibromatosis of the nerves of the skin associated with multiple pigmented nevi of the skin. The nevi of the lower extremities were symmetrically distributed. No abnormal pigmentation was present in the eyes, kidneys, adrenals or other viscera.

Berblinger [20] considered the pigmented neoplasm of the brain as a lesion independent of those of the skin. The pigmented nevus was of a complex type. Besides the nests of nevus cells in the upper portion of the corium, there were large tracts of cells or funiculi in the lower portion of the corium and in the hypoderm. He agreed with Wieting and Hamdi,[21] who considered the production of pigment a characteristic of the epithelium alone. In consideration of all the changes which had taken place in this case, Berblinger was unable to explain the cutaneous neurofibroma and the sarcomatosis of the leptomeninges. He was familiar with Soldan's [22] observations on the common association of neurofibromatosis of the nerve-endings with pigmented nevi, but he was not able to verify these observations in his case. He could not reduce all the changes to the simple formula of developmental disturbances in the germinal layer, namely, the ectoderm.

Farnell and Globus [23] made a thorough review of the literature pertaining to primary melanoblastoma of the central nervous system and reported a case of primary melanoblastosis of the leptomeninges and brain. In this case there were numerous pigmented moles of varied size scattered over the trunk and extremities; however, none showed clinical evidence of malignant degeneration, and autopsy did not reveal melanotic tumors of the viscera.

These authors did not agree with the view of Ribbert [24] and other earlier writers that all melanotic tumors of the central nervous system are secondary to melanotic growth of the skin or to other normal accumulations of pigment cells. They expressed the belief that since multiple unrelated tumor formations of divergent types frequently occur in a patient, it is not unreasonable to suppose that independent yet similar pigmented malformations may occur in the patient's different organs.

Similar congenital anomalies which simultaneously involve different organs can be correlated only when the involved structures are known to arise from the same germinal layer. It is conceivable that developmental disturbances in the ectoderm occurring early in the life of the zygote might produce similar yet independent congenital malformations in the skin and in the central nervous system. The interpretation of

21. Wieting and Hamdi, cited by Berblinger.[20]

22. Soldan, cited by Ewing.[26]

23. Farnell, F. J., and Globus, J. H.: Primary Melanoblastosis of Leptomeninges and Brain, Arch. Neurol. & Psychiat. **25**:803 (April) 1931.

24. Ribbert, cited by Farnell and Globus.[23]

the relationship between the nevi and the pigmentary condition in the nervous system in cases similar to the one reported here embraces many intricate problems relative to the origin of the pigmented nevus and to the embryologic development of the meninges.

The epidermal theory of Unna until recent years has been the most acceptable explanation of the origin of the pigmented nevus. Masson [25] advanced the hypothesis that nevi originated from special cells of the tactile nerve endings. Although this theory had been suggested by Soldan,[22] Masson's observations were original and more convincing. Improved methods of tissue fixation and staining were used by Masson in his investigations. He showed that nevi result from proliferation of elements of the ends of the cutaneous tactile or sensory nerve. He observed many nerve fibrils in and arborized about the groups of nevus cells, and he was able to trace the superficial nevus cell from the tactile corpuscle of Merkel and Ranvier through its various transitional stages to nevoid tactile corpuscles in the corium that resemble the Wagner-Meissner corpuscles. These corpuscles were, in turn, connected with the deeply seated, elongated nevus cells. This syncytium was observed to be continuous with the medullated nerves of the skin. Masson [2] expressed the belief that the nevus cells have the essential characteristics of the Schwann cell, that the nevus is a neuroma, and that in some instances neurinomas may occur at the same time.

Although the theory of the nervous origin of nevi has not been universally accepted, it has the support of Ewing,[26] Foot [27] and Becker.[28] In an effort to prove that a melanoma can arise primarily in the meninges and to obtain additional evidence for the theory of a nervous rather than a dermal origin of nevi, Foot and Zeek [1] made a special study in two cases of primary melanoma of the meninges. These authors reasoned that since Maximow and other histologists have stated that many nerves of the meninges end in organs similar to the Wagner-Meissner corpuscles, the origin of melanoma of the meninges might be analogous to that of melanoma of the skin. It is obvious that there is no plausible explanation for the epidermal origin of primary melanoma of the meninges. Virchow [17] traced the derivation of the primary melanoma of the central nervous system to the physiologic chromatophore of the meninges. This view has been accepted by many other authorities.

---

25. Masson, P.: Les naevi pigmentaires, tumeurs nerveuses, Ann. d'anat. path. **3**:417 (May); 657 (July) 1926.

26. Ewing, J.: Problems of Melanoma, Brit. M. J. **2**:852 (Nov. 22) 1930.

27. Foot, N. C.: On Silver Impregnation of Melanotic Tumors, Am. J. Path. **7**:619 (Nov.) 1931.

28. Becker, S. W.: Origin and Nature of Pigmented Nevi (Schwannomas), Arch. Dermat. & Syph. **30**:779 (Dec.) 1934.

Foot and Zeek made a careful study of their material with special methods of silver impregnation. These authors observed fibrils similar to those seen in pigmented nevi, which branched and arborized about the cells in the tumor nests. They expressed the belief that this observation presented strong evidence in favor of Masson's theory of the nervous origin of melanoma, but they reserved final conclusions until they made a more intensive study.

If one accepts Masson's theory that nevi arise from the cells of the sheath of Schwann, what embryologic observations have been made that may have value in the interpretation of the relationship which may exist between an extensive benign pigmented nevus and primary melanoma of the meninges?

It is accepted that the epidermis and the parenchyma of the nervous system arise from the common germinal layer, the ectoderm; however, the embryologic development of the meninges is still debated. The orthodox view has been that the meninges arise mainly from the mesoderm; however, several recent reports in the literature attribute the origin of the dura to the mesoderm and that of the leptomeninges to the ectoderm.

The sheath of Schwann of the peripheral nerves, which lies next to the inner or myelin sheath, is considered to be of ectodermal origin.[29] Nageotte [30] stated that the neuro-ectodermal emigration from the neural crests which is destined to form the spinal nerves leaves along its track chains of cells which mark the course of the future posterior roots. These cells are regarded by Harrison [31] as embryonic Schwann cells.

According to Nageotte,[30] Masson and Oberling expressed the belief that the neuro-ectodermal migration which gives rise to the Schwann cells also produces the cells of the arachnoid, thus accounting for the structural similarity between tumors of the arachnoid and those of the nerve.

Harvey and Burr [32] contended that the pia-arachnoid arises from the neural crests and is analogous to the neurolemma or sheath of Schwann of the peripheral nerves. In experiments with embryos of Amblystoma punctatum at a certain stage of development, these authors transplanted portions of neural tube with and without the neural crests,

29. Masson, P.: Experimental and Spontaneous Schwannomas (Peripheral Gliomas), Am. J. Path. **8**:367 (July) 1932.

30. Nageotte, J.: Sheaths of the Peripheral Nerves, Nerve Degeneration and Regeneration, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 1, p. 189.

31. Harrison, R. G.: Neuroblast Versus Sheath Cell in the Development of Peripheral Nerves, J. Comp. Neurol. **34**:123, 1924.

32. Harvey, S. C., and Burr, H. S.: Development of Meninges, Arch. Neurol. & Psychiat. **15**:545 (May) 1926.

and they observed that in the transplants without the neural crest the pia-arachnoid failed to develop while in those with the neural crest it developed in a normal way. Their observations are significant in respect to neoplasms of the pia-arachnoid. They expressed the belief that on further study many tumors of the meninges, ganglions, sympathetic nervous system and peripheral nerves may be placed in a common group of neoplasms which arise from the cells of the neural crest.

In a subsequent report by Harvey, Burr and Van Campenhout,[33] additional observations were offered in substantiation of their original conclusions. Weed [34] expressed the belief that the work of these authors is not conclusive. In discussing the presentation of Harvey and Burr,[32] Cushing [7] expressed the opinion that a common origin of the sheath of the nerves and of the arachnoid would help in explaining the occurrence of multiple tumors of the meninges which are occasionally seen in Recklinghausen's disease. He expressed the belief that these tumors develop from the arachnoid rather than from the dura, and he suggested that in this disease one may be dealing with a neoplastic disorder which is due to congenital derangement of the entire system.

COMMENT

The case reported in this paper is an instance of an unusually large, complex pigmented nevus of the skin and associated diffuse melanoblastosis of the leptomeninges of the brain and the spinal cord. The important question arises whether the pigmented changes in the meninges are related to the pigmentation of the skin.

Three possibilities should be considered in the interpretation of these observations: (1) that the melanoma of the meninges is a metastatic tumor arising from the nevus or from the eye, either of which is the usual location of a primary malignant melanoma; (2) that the lesions differ in type, that they are unrelated and that their association is coincidental, and (3) that the nevus and the changes in the nervous system are related in that they are congenital malformations resulting from a widespread developmental disturbance in the ectoderm.

Although a complete autopsy was not permitted, there is some justification for assuming that the first premise is not applicable in this case. There was no clinical evidence of malignant degeneration in the nevus, nor were there signs or symptoms suggesting a primary lesion in the eye or secondary involvement of the viscera. The observations of Virchow,[17] Boit,[19] Grahl [18] and Farnell and Globus [23] in similar cases

33. Harvey, S. C.; Burr, H. S., and Van Campenhout, E.: Development of Meninges: Further Experiments, Arch. Neurol. & Psychiat. **29**:683 (April) 1933.

34. Weed, L. H.: The Meninges, with Special Reference to the Cell Coverings of the Leptomeninges, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 2, p. 611.

in which there was lack of involvement of tissues other than the skin and nervous system give weight to my negative clinical observations. The definite limitation of the diffuse cellular infiltration to the pia-arachnoid is contrary to the usual observation in a case of metastatic melanoma of the central nervous system. Metastatic melanomas occur as disseminated or solitary nodules in the brain or the viscera which they involve. It is not probable that metastasis would become so diffuse and evenly distributed throughout the meninges without involving the parenchyma of the brain or spinal cord.

The second possibility cannot easily be accepted unless one favors the epidermal theory of the origin of nevi and the concepts of the mesodermal origin of the pia-arachnoid and the derivation of primary melanomas of the meninges from chromatophores. These concepts have been recognized for several years.

The third possibility seems to be the most plausible, especially if one accepts Masson's theory of the origin of nevi and the yet uncorroborated work of Harvey and Burr [32] and Foot and Zeek.[1] Unfortunately, the fixation of the material in the present instance prevented the use of Masson's technic; however, the structure of the nevus in this case is similar to that of the giant neuronevus which Masson described.

The greatest difficulty is in explaining the origin of the primary melanoma of the meninges in correlation with the theory of the nervous origin of the pigmented nevus of the skin. If it is eventually determined that the pia-arachnoid and the sheath of Schwann have a common origin from the neural crest, as suggested by Harvey and Burr,[32] there will be justification for considering the changes in the skin and nervous system in such cases as the present one to be related congenital malformations. In support of this assumption, one should consider the clinical evidence in the occurrence of multiple tumors of the arachnoid in cases of Recklinghausen's disease and of the angiomas of the meninges in association with vascular nevi in the same neuromere.

It may be argued in this case that a congenital nevoid change in the pia-arachnoid underwent hyperplasia or relatively benign malignant alteration which spread throughout the leptomeninges, or that a neoplasm arose from the neuro-ectodermal tissue of the arachnoid similar to the development of moles from the nerves during adult life. In this instance the diffuse and extensive involvement of the pia-arachnoid interfered with absorption of the cerebrospinal fluid sufficiently to cause fatal hydrocephalus.

SUMMARY AND CONCLUSIONS

A rare case of an extensive pigmented nevus associated with primary diffuse melanoblastosis of the meninges is reported. The correlation of these observations is difficult and depends on the ultimate

solution of the origin of nevi and of the debated questions concerning the embryologic development of the meninges. It is possible that the nevus and the changes in the meninges are related congenital malformations resulting from early developmental disturbances in the ectoderm and that such lesions may be considered as filling the gap which exists between extensive benign melanomas of the skin and primary melanoma of the meninges.

ABSTRACT OF DISCUSSION

Dr. Fred D. Weidman, Philadelphia: At the Chicago meeting of the American Medical Association, Dr. Eiman and I reported a case similar to this, but the paper was never published. Probably 35 per cent of the body of the child was covered with a pigmented verrucous nevus. She died of cerebrospinal complications, including convulsions. Dr. Eiman and I expressed the belief that the two sets of nevi were referable to their derivation from a common source, namely, the ectoderm. At that time Masson's work was not familiar; now I am glad to agree with Dr. Netherton's theory of the development of these tumors.

The practical point that has remained with me ever since is the menace in all cases of extensive cutaneous nevi of their further future development in the cerebrospinal system. I have been hoping for the opportunity to study another tumor of this sort, when I could make a spinal puncture and determine whether any significant substance, such as melanogen, could be found in the fluid by laboratory methods. In the case of the child on whom I reported there were no ocular symptoms. In a fleeting glance of one of the lantern slides showing tumor tissue in the present case, I thought I saw a rosette-like arrangement of some of the cells. A type of neuro-epithelioma of the retina is characterized by formation of rosettes.

Dr. E. W. Netherton, Cleveland: The case I have reported seems to me to be of importance in an attempt to correlate primary melanoma of the meninges, which occurs rarely, and extensive pigmented nevi of the skin. It is obvious that a primary malignant melanoma cannot be considered to arise from epithelium. The theory of the nervous origin of nevi seems to be the most plausible of the theories so far advanced. If this theory is accepted there is a basis for an attempt to correlate the two conditions. I wish to emphasize that in cases of this type might exist the link between the extensive pigmented nevi of the skin and primary melanotic tumors of the meninges. The ocular findings in the present case were increased tension and hemorrhage in the right eye. The eye was not dissected and studied histologically.

HODGKIN'S DISEASE OF THE SCALP

REPORT OF A CASE

NORMAN M. WRONG, M.B.

TORONTO, CANADA

In 1934 a case was reported by Greenhouse and Cornell [1] in which the condition was designated "lymphoblastoma (Hodgkin's disease) of the scalp." Because of its similarity to their case another case is reported here.

Considering its rarity, Hodgkin's disease has commanded a large share of attention in the literature. One of the most recent and most comprehensive reviews of the whole subject is by Wallhauser,[2] who gave its incidence at 0.16 per cent in 8,485 autopsies. Cole,[3] Fox,[4] Miller,[5] Rulison [6] and Lisa [7] are only a few of the authors who have written extensively on the subject of Hodgkin's disease of the skin.

Cole's [3] description of the manifestations in the skin, without the formation of tumors, has been much quoted by later writers. This nonspecific involvement of the skin occurs in about 25 per cent of the cases, and Lisa stated that in 10 per cent the cutaneous symptoms were the presenting ones. On the other hand, nodules or tumors in the skin with the characteristic histologic picture of Hodgkin's disease are extremely uncommon. Hoevelborn, cited by Greenhouse and Cornell,[1] found sixty-eight cases reported in the literature to 1932. In most of the cases in which there are specific lesions in the skin, the lesions are secondary to or accompanied by Hodgkin's disease of the lymphatic glands or viscera, although there is not necessarily extension from deep structures to the skin. The diagnosis of Hodgkin's disease of the skin

---

From the Department of Medicine, University of Toronto, and the Hospital for Sick Children.

Read at the joint session of the American Medical Association and the Canadian Medical Association, Atlantic City, N. J., June 14, 1935.

1. Greenhouse, C. A., and Cornell, V. H.: Lymphoblastoma (Hodgkin's Disease) of Scalp: Report of Case, Arch. Dermat. & Syph. **29**:569 (April) 1934.

2. Wallhauser, A.: Hodgkin's Disease, Arch. Path. **16**:522 (Oct.); 672 (Nov.) 1933.

3. Cole, H. N.: Cutaneous Manifestations of Hodgkin's Disease, J. A. M. A. **69**:341 (Aug. 4) 1917.

4. Fox, H.: Lymphogranulomatosis of the Skin in Hodgkin's Disease, Arch. Dermat. & Syph. **2**:578 (Nov.) 1920.

5. Miller, H. E.: Lymphogranulomatosis Cutis: Hodgkin's Disease, Arch. Dermat. & Syph. **17**:156 (Feb.) 1928.

6. Rulison, R. H.: Hodgkin's Disease of Skin: Report of Case, Arch. Dermat. & Syph. **22**:389 (Sept.) 1930.

7. Lisa, J. R.: Hodgkin's Disease of Skin: Report of Case, Arch. Dermat. & Syph. **26**:268 (Aug.) 1932.

in cases without apparent glandular involvement is so brave as to be almost foolhardy. In the case reported by Greenhouse and Cornell,[1] the histopathologic findings suggested Hodgkin's disease, and in the case reported here it is hoped that the histopathologic description and diagnosis and the photomicrographs will suggest that there is at least a strong resemblance to Hodgkin's disease.

REPORT OF CASE

History.—D. A., a boy aged 12 years, born in Canada of English parents, had been in good health previous to June 1931. Following slight trauma to the left parietal region, a small, firm nodule the size of a hickory nut was noticed in the area. It increased in size gradually, and the hair became sparse over it. The patient came to the outpatient dermatologic clinic at the Hospital for Sick Children, Toronto, in February 1932, and a small elliptic piece was removed from the center of the lesion for microscopic examination. A provisional diagnosis of scleroderma was made before the specimen for biopsy was taken.

Examination.—The patient did not report at the clinic again until November 1932, and at that time the lesion measured 10.5 by 7.5 cm. and was elevated about 1 cm. above the surrounding skin. It was firm, rounded and smooth, and moved as a whole freely over the underlying bone. It felt warmer than the surrounding skin, and the surface was covered with numerous fine, dilated blood vessels. There were a few long hairs and many fine ones. The lesion was not tender to light or heavy palpation and had never been ulcerated. The only scarring present was that left by the removal of tissue for biopsy (fig. 1). Five small, hard lymphatic glands were felt in the left posterior triangle of the neck. The lymphatic glands elsewhere were not enlarged, nor was the spleen palpable. A general examination of the patient revealed nothing unusual.

The Wassermann and Kahn reactions of the blood were negative. Examination of the blood revealed: hemoglobin, 81 per cent; erythrocytes, 4,800,000, and leukocytes, 10,300. The differential blood count revealed: neutrophils, 47 per cent; lymphocytes, 52 per cent, and endothelial cells, 1 per cent. The lymphocytes appeared to be normal adult cells.

Histopathologic Reports.—The initial histopathologic study was made by Dr. I. H. Erb, of the Hospital for Sick Children, Toronto, whose report was as follows:

"The gross specimen consisted of an elliptic piece of hair-bearing skin 2.5 cm. long by 0.8 cm. wide, the under-surface of which was composed of a fairly firm, pinkish, lobulated tissue. Microscopically, the surface epithelium, hair follicles, sebaceous and coil glands appeared normal. In the subcutaneous tissues and infiltrations the true skin was a cellular mass arranged in the form of numerous small nodules of various sizes, partly surrounded and separated from one another by a connective tissue stroma (fig. 2). In some instances the connective tissue surrounding the nodules formed a thick zone; in others it was present only as a delicate structure, and some of the cells appeared young. Many of the nodules showed, immediately inside the zone of connective tissue, a band of small round cells which stood out in contrast to the larger cells of which the nodules were for the most part composed. The larger cells were round or slightly oval, with scanty cytoplasm, and showed marked variation in size, some of the larger ones having from five to six times the diameter of a lymphocyte (fig. 5). The nuclei were vesicular, and some of them were indented. Here and there one could see large multinucleated cells of the Dorothy Reed type (figs. 3 and 4). Mitotic figures

Fig. 1.—Photograph taken in November 1932 previous to treatment. The biopsy scar may be seen at *a*. The picture does not properly indicate the elevation of the lesion above the surrounding skin.

Fig. 2.—Section of biopsy specimen under low power magnification, showing the relation of the tumor infiltrate to the dermis and epidermis; × 24.

were plentiful, and some of them had rather abundant, fairly granular, pale-staining cytoplasm (fig. 5). Scattered throughout the specimen could be seen a few lymphocytes with an occasional polymorphonuclear leukocyte, but no eosinophils could be found.

"While the general structure and the cellular picture bore a striking resemblance to those of Hodgkin's granuloma, the location was rather unusual, and the subsequent history of well-being over a period of three years makes one wonder whether or not this is the correct diagnosis."

A section was sent to Professor James Ewing, of the Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York, and he was asked for his opinion as to the diagnosis. Professor Ewing reported as follows:

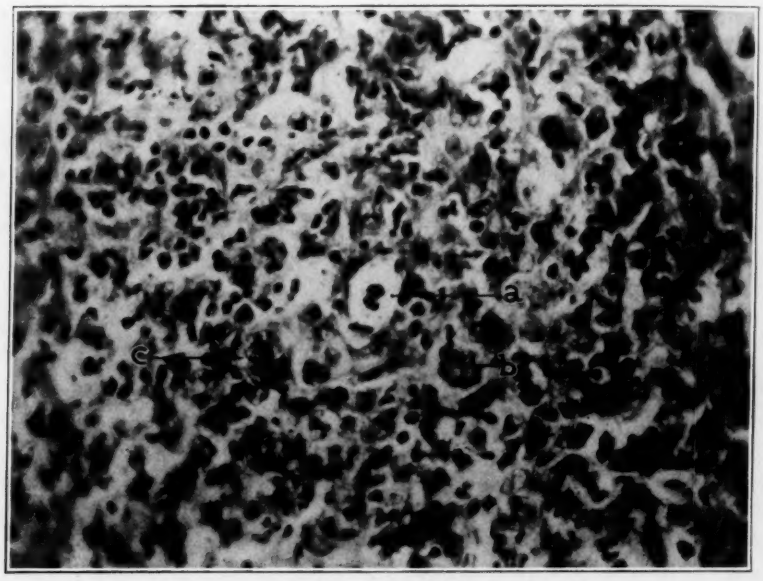

Fig. 3.—Section showing the polymorphous nature of the infiltrate. At *a* is seen a mitotic figure, at *b* a large mononuclear cell and at *c* a giant cell of the Reed-Sternberg variety; × 320.

"In the case of D. A., I am inclined to think that the condition in the scalp is Hodgkin's disease of a hyperplastic type. The setting is extremely unusual, but the histologic picture is rather characteristic. Dr. Stewart agrees with me in the diagnosis."

Treatment and Progress.—The patient was referred to the roentgenologic department of the Hospital for Sick Children for treatment, and on November 30 and on December 6 and 13 the following dosage was given to the lesion on the scalp only: five minutes' irradiation with 5 milliamperes with an 8½ inch (21.6 cm.) gap, equivalent to 90 kilovolts, at a distance of 10 inches (25.4 cm.) with a 5 mm. aluminum filter (total dose, 100 roentgens). One week after the first treatment, the lesion was paler and smaller, and on December 13, the day the third dose was given, it measured only 8.5 by 5 cm., was pale, had become much flatter, so that there was little elevation above the surrounding skin, and was no longer of firm consistency.

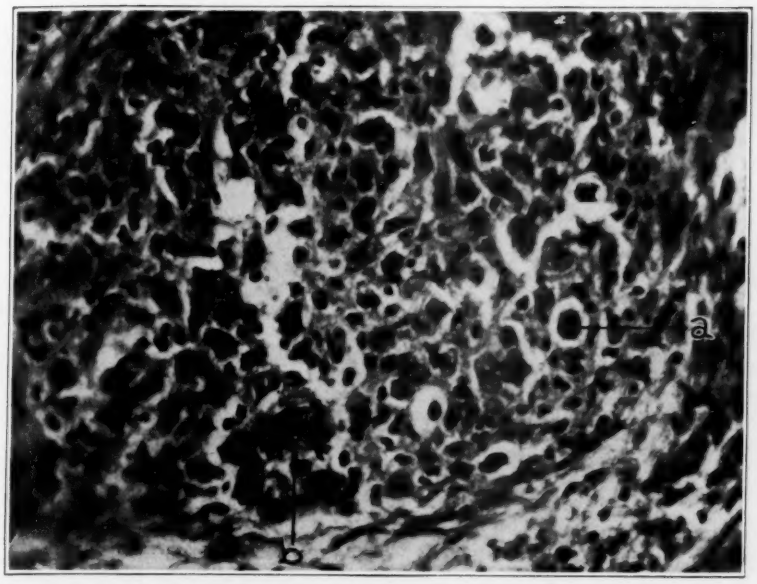

Fig. 4.—Section showing at *a* the mononuclear variety of the Reed-Sternberg cell and at *b* the multinucleated type; × 350.

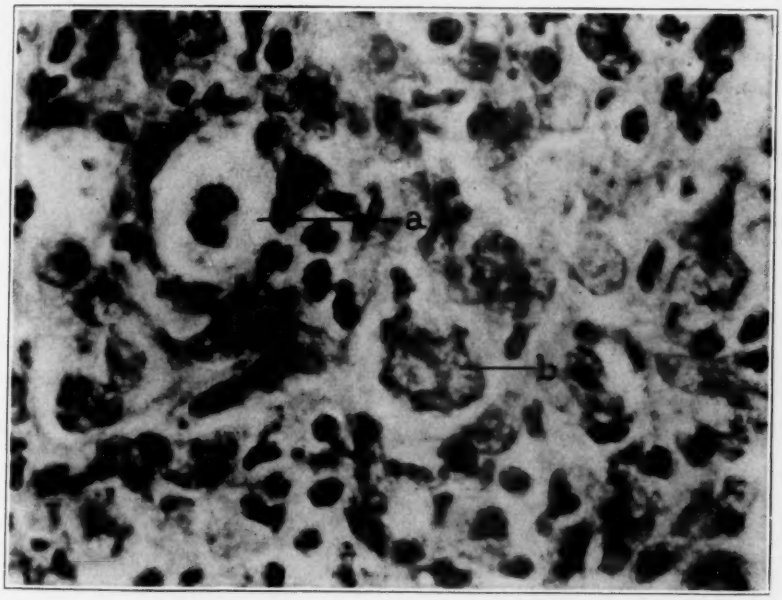

Fig. 5.—Part of the section shown in figure 3, highly magnified, to show in more detail the mitotic figure at *a* and the large mononuclear cell of the Reed-Sternberg type at *b*; × 800.

On Jan. 14, 1933, the involved area appeared normal except for partial baldness and slight pigmentation. The lymphatic glands were no longer palpable.

On Jan. 28, 1933, examination of the blood revealed: hemoglobin, 100 per cent, and leukocytes, 9,900. The differential blood count was: neutrophils, 53 per cent; lymphocytes, 44 per cent, and endothelial cells, 3 per cent. All the cells appeared to be normal adult cells.

On March 4, 1933, the patient was in excellent condition generally. The lesion was almost completely covered with hair and was flat, and the skin and subcutaneous tissues felt normal. The lymphatic glands were not palpable.

On Jan. 24, 1935, the patient weighed 124½ pounds (56.47 Kg.). His general condition was excellent. He played football and hockey and experienced no ill effects from violent exercise. The tuberculin reaction was negative. A roentgen examination of the chest revealed no abnormalities. The affected area showed slight redness. The hair was sparse over it. No thickening was noted in the skin or subcutaneous region. The lymphatic glands were barely palpable in the anterior and posterior cervical regions and in the groin, but not in the axillae. The liver and spleen were not palpable. There was no evidence of Hodgkin's disease. Examination of the blood revealed: hemoglobin, 86 per cent; erythrocytes, 5,770, and leukocytes, 2,800. The differential blood count revealed: lymphocytes, 56 per cent; neutrophils, 38 per cent; eosinophils, 4 per cent, and large mononuclears, 2 per cent. The red cells, platelets and leukocytes appeared normal.

DIFFERENTIAL DIAGNOSIS

Leukaemia cutis.—In view of the relative lymphocytosis, lymphatic leukemia must be considered. The lymphocytes in the blood smear appeared as normal adult cells, however, and a lymphocyte count of 50 per cent for a boy of 12 years is not exceptional. The histologic picture did not suggest leukaemia cutis.

Spiegler-Fendt's sarcoid.—In the four cases of this sarcoid presented by Lewis [8] none of the papules was larger than a split pea in size. There was nothing comparable to the 10 cm. plaque present on the scalp in the case described here. The histologic picture was somewhat similar in that there were epithelioid cells and lymphocytes grouped in islands, but in sarcoid the primary focus seems to be in the upper portion of the dermis with extension into the hypoderm, whereas in the case presented here the chief involvement was in the hypoderm with the lower and middle portions of the dermis tending to be infiltrated. There was no formation of new vessels or proliferation of vessel walls such as is seen in Spiegler-Fendt's sarcoid, but the Reed-Sternberg cells characteristic of lymphogranulomatosis were present.

Other Diseases.—Syphilis and tuberculosis were considered, but speedily rejected in view of the clinical and laboratory data, and scleroderma, the original diagnosis, was excluded by the histologic appearance.

---

8. Lewis, G. M.: Is Spiegler-Fendt Sarcoid a Clinical or Histologic Entity? Arch. Dermat. & Syph. **31**:67 (Jan.) 1935.

COMMENT

There are many arguments against the diagnosis of this case as one of Hodgkin's disease, chief of which are the absence of glandular involvement, the healthy condition of the patient four years after the onset, the complete disappearance of the lesion after three small doses of roentgen rays and, finally, the fact that the histopathologic diagnosis of Hodgkin's disease is by no means always accurate.

On the other hand, the fact must be borne in mind that there was a progressively growing tumor on the scalp. The tumor literally melted away following three small doses of filtered roentgen rays. It is well known that the tumors of Hodgkin's disease are very radiosensitive. On histologic examination, two pathologists independently have expressed the view that the section strongly suggests Hodgkin's disease.

The patient was only 10 years of age at the time of onset of the disease. Cases have been reported in patients much younger than this, and of Ziegler's [9] series of two hundred and twenty patients, 16.8 per cent were in the second decade of life. The disease is more malignant in children than in adults, and the average duration of life after the onset of the symptoms is only twenty-one months. However, Cunningham, cited by Wallhauser,[2] reported a case in which the patient lived for twenty-five years. Smith [10] stated that cutaneous manifestations are comparatively infrequent in childhood. He collected reports of one hundred and eight cases in children, of whom eighty-eight were boys.

Corbeille [11] found that examination of the blood revealed nothing striking. Feer, quoted by Smith,[10] stated that leukocytosis is seldom marked in children but that leukopenia is more common in adults while the monocytes are more numerous. The absence of eosinophilia in the blood and in the histologic section is by no means unique. The proportion of eosinophils seems to vary directly as the degree of irritation of the skin.

The similarity of the case reported here to the one reported by Greenhouse and Cornell [1] is pronounced. In both there were firm, painless plaques on the scalp with loss of hair over the area. In each there was rapid and complete disappearance of the symptoms on the application of comparatively small doses of roentgen rays. In neither was there glandular or visceral involvement, changes in the blood or progressively failing health. That the two cases are instances of Hodgkin's disease is certainly open to doubt. There is, however, slight doubt that they rep-

9. Ziegler, K.: Ueber die Hodgkinsche Krankheit, das maligne Lymphogranulom, Berl. klin. Wchnschr. **48**:1917, 1911.

10. Smith, C. A.: Hodgkin's Disease in Childhood, J. Pediat. **4**:12 (Jan.) 1934.

11. Corbeille, C.: Hodgkin's Disease in Children: Clinical Study of Thirty-Three Cases, Minnesota Med. **11**:678 (Oct.) 1928.

resent a cutaneous manifestation of a similar disease entity which is closely allied, at least histologically, to Hodgkin's disease.

SUMMARY

The case is reported of a boy of 12 years who had a flat tumor in his scalp. After the administration of three small doses of roentgen rays the tumor disappeared.

A biopsy made before treatment revealed a histopathologic picture suggestive of Hodgkin's granuloma.

The case is believed to be similar to the one reported by Greenhouse and Cornell.[1]

ABSTRACT OF DISCUSSION

DR. RICHARD W. FOWLKES, Richmond, Va.: Dr. Wrong's diagnosis is probably correct, but in view of the knowledge, or rather lack of knowledge, about the lymphoblastomas and sarcomas, I consider it dangerous to record this case and the case reported by Greenhouse and Cornell as being correctly diagnosed. Several workers have shown that individual tumors of the group, although apparently definite, histologically, may undergo transition and become transformed into another clinical or histologic entity. Furthermore, a histologic interpretation by a large number of experts in a given case is rarely unanimous.

Last year Ginsburg (*Ann. Int. Med.* **8**:14 [July] 1934) gave a splendid summation of the literature from 1832, when Hodgkin first described the clinical picture, down to the present. With this additional evidence, it is quite convincing to my mind that Hodgkin's disease and lymphosarcoma are one and the same condition. At the end of his study he said, "Biologically, therefore, Hodgkin's disease varies in no fundamental characteristic from lymphosarcoma. Whatever variations it may present at times are merely variations that one would expect to find in any disease affecting different individuals under different constitutional and environmental conditions."

In 1923 Arzt of Riehl's clinic reported a case of "Hodgkin's disease d'emblée of the scalp." The first tumor appeared in the occipital region, grew larger and ulcerated. Early in the case examinations of tissue showed the picture of so-called Hodgkin's disease. A definite clinical generalization of the disease developed progressively in the patient, and at necropsy the original diagnosis of Hodgkin's disease was confirmed.

Dr. Wrong is to be congratulated on his early biopsy and treatment which resulted in the absorption of the tumor. It is possible that he saved his patient from the sequence of events reported by Arzt. I am sure that he will follow the child for a period of years with great interest.

MYCOSIS FUNGOIDES WITH POIKILODERMA-LIKE SYMPTOMS

EDWARD A. OLIVER, M.D.
CHICAGO

Within the last few years increasing attention has been given the cutaneous picture poikiloderma atrophicans vasculare. A number of articles on this subject have appeared in the foreign journals, and published transactions of proceedings of dermatologic societies in this country show a number of cases presented with that diagnosis.

Among authorities there is considerable difference of opinion as to what symptoms represent the picture of poikiloderma atrophicans vasculare. Some authors doubt whether it is a separate disease, while others believe firmly that it is a definite clinical entity with a clearcut symptomatology. It is not generally known that poikiloderma-like symptoms may be part of the picture of many chronic inflammatory dermatoses, and this probably is the reason why so many patients are now being shown with poikiloderma as the diagnosis. Dr. Otto H. Foerster, in 1931, first called attention to this fact.

The following report deals with the clinical study of a patient belonging to this category. When first seen and examined he presented many of the symptoms of poikiloderma. While I never believed that his case was one of poikiloderma, the clinical picture that he displayed justified the diagnosis of idiopathic atrophy with poikiloderma-like symptoms, and he was shown at several society meetings with that diagnosis. He was seen from time to time and repeatedly examined, but at the time of his last visit the increase in the severity of the symptoms and an examination of new specimens taken for biopsy gave definite evidence that the condition was a rather unusual manifestation of mycosis fungoides.

REPORT OF A CASE

J. W., a white man aged 42, a lawyer, was first seen by me on Dec. 7, 1932, with a rather unusual cutaneous eruption, distributed in patches over the back, buttocks, sides of the trunk, arms and thighs. From a distance the lesions appeared much like patches of chronic radiodermatitis. On close examination, however, the resemblance was seen to be a superficial one. There were four large patches on the back, one on the right buttock, one on the extensor aspect of the upper part of the right arm, one on the inner aspect of the left forearm, one below the nipple on the right side of the chest, two large ones involving the anterior aspect

Read at the Fifty-Eighth Annual Meeting of the American Dermatological Association, Inc., White Sulphur Springs, W. Va., May 3, 1935.

of the thighs and two small areas just below the popliteal spaces on the posterior aspect of the legs.

The largest patch was in the left renal region and when first seen measured 6 by 6½ inches (12 by 13.5 cm.) and was reddish brown. The skin of this area was dry, scaling, atrophic, beset with small hemorrhagic puncta and covered with hypertrophic crusts and scales, arranged in an annular configuration. The area on

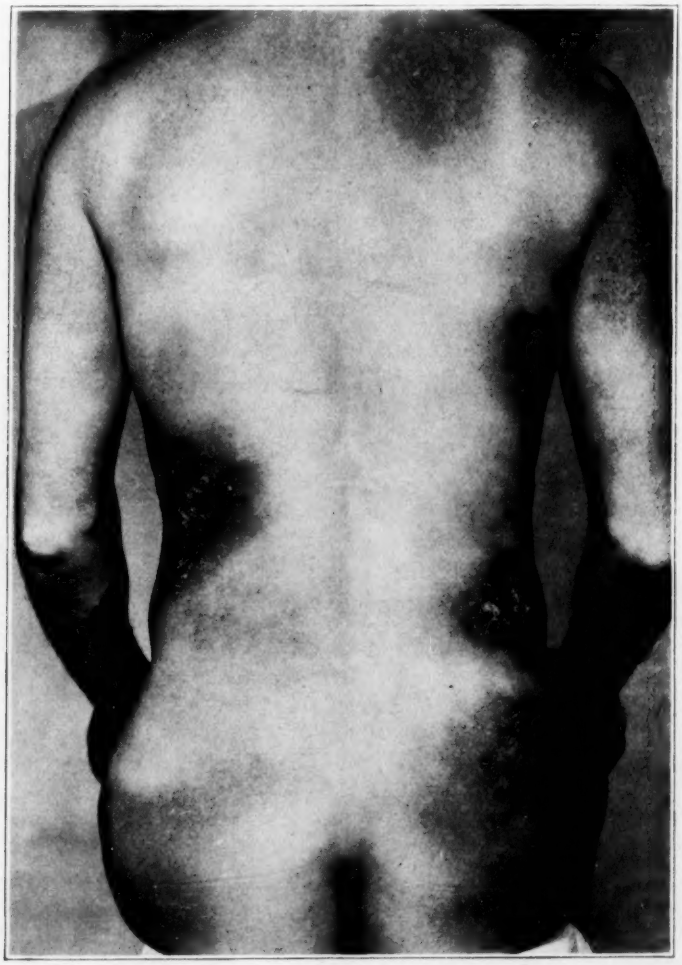

Fig. 1.—Photograph of the patient at the first visit, showing the large, isolated, atrophic areas which resembled areas of chronic roentgen ray dermatitis.

the right flank measured 3 by 3½ inches (7.5 by 9 cm.) and was of the same appearance as on the left, except that the crusting was not so marked. The lesion on the extensor aspect of the upper part of the right arm measured 3 by 3 inches. The skin here was very atrophic, wrinkled and dry and was covered with adherent scales. It also was the seat of numerous hemorrhagic puncta. The other lesions varied in size. One below the right nipple was saucer-shaped and

measured 6 by 6 inches; one on the right buttock measured 3 by 3 inches, while most of the other lesions except those on the thighs were smaller. Those on the thigh measured 5 by 5 inches (12.7 by 12.7 cm.). The skin in all the involved areas displayed the same characteristics. At a distance the patches looked like areas of chronic radiodermatitis, but on close examination they were seen to be dark reddish brown, dry, and atrophic and the seat of some scaling and numerous

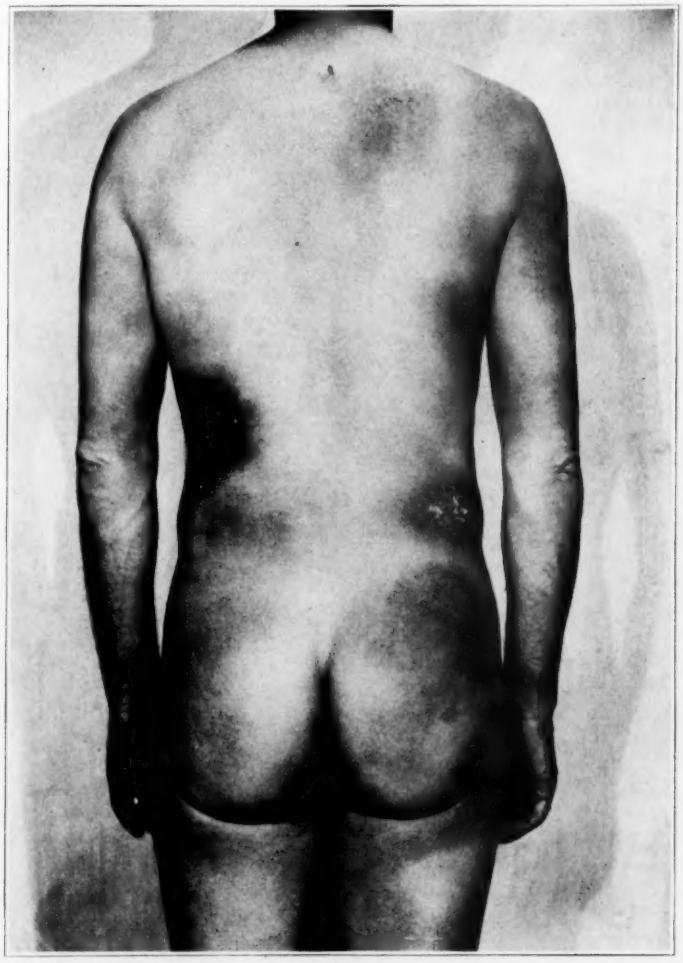

Fig. 2.—Photograph of the patient at the first visit, showing the extent of the eruption on the posterior aspect of the body.

cayenne pepper-like spots. There was no pruritus. The patient's chief complaint was that in cold weather his skin became so dry that it was necessary to keep it constantly greased. There was some puffiness of the skin below the eyes; it was erythematous and the seat of a slight amount of scaling. There was no leukoplakia, but a point of added interest was the presence of three striae about ¼ inch (0.6 cm.) in width running transversely across the back in its midsection.

The patient stated that the condition began about seven years before, as a dry ichthyotic condition on the lower part of both legs, which had gradually extended up the posterior aspect of both legs. The patch on the left side, which was the first to appear, had begun to develop three years ago.

He was a large, well nourished man, 6 feet and 1 inch (185.4 cm.) in height. His weight was 182 pounds (82.6 Kg.). His general health had always been

Fig. 3.—Close-up view of the large plaque on the left flank, showing beginning crusts and vegetations.

good. While serving overseas with the army, he had suffered an attack of influenza. He had also had all the ordinary infectious diseases of childhood, but to his knowledge there had never been any cutaneous disease in the family. The blood pressure was 132 systolic and 70 diastolic. The basal metabolic rate was 0, and on roentgenographic examination the shadows representing the bony structure forming the sella turcica were found to be within normal limits. There was no

evidence of bridging, erosion or tumors. The tonsils had been removed, and there was no evidence of infection in the teeth. The prostate was normal.

Urinalysis showed a specific gravity of 1.025; albumin, 0.05 per cent; absence of sugar, a few leukocytes and considerable mucus. A blood count showed 5,600,000 red cells, 8,100 white cells and 82 per cent hemoglobin. A differential

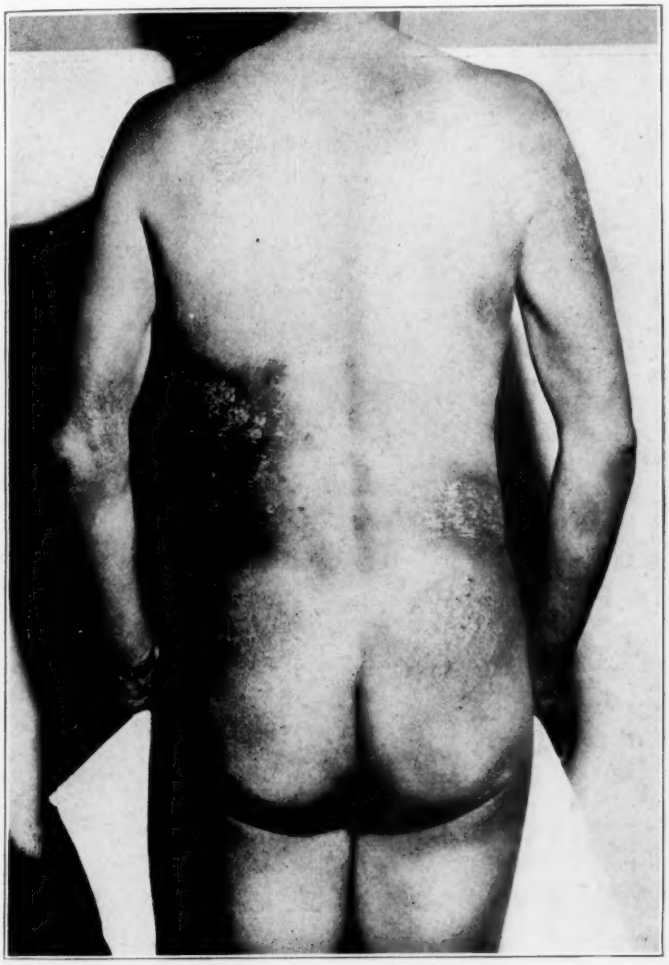

Fig. 4.—Photomicrograph of one of the first sections, showing epidermal atrophy, parakeratosis and superficial micro-abscess formation in the epidermis, and dense cellular infiltration in the corium, blending with the basal layer of the epidermis. Magnified 100 diameters.

count showed small mononuclear lymphocytes, 27 per cent; polymorphonuclears, 58 per cent; monocytes, 9 per cent; neutrophils, 0.7 per cent, and eosinophils, 6 per cent. The Wassermann, Kolmer and Kahn reactions were all negative.

Histologic Examination.—Small pieces of tissue were excised from atrophic spots on the left and right flanks and submitted to histologic examination. The sections examined showed a uniform epidermal atrophy, the result of pressure from the underlying infiltrate. The rete pegs and papillae were almost uniformly obliterated, leaving only a straight line. Exclusive of the horny layer, the epidermis in most places was but half a dozen cells in depth. The stratum granulosum, though absent in places, was of approximately normal appearance. The stratum

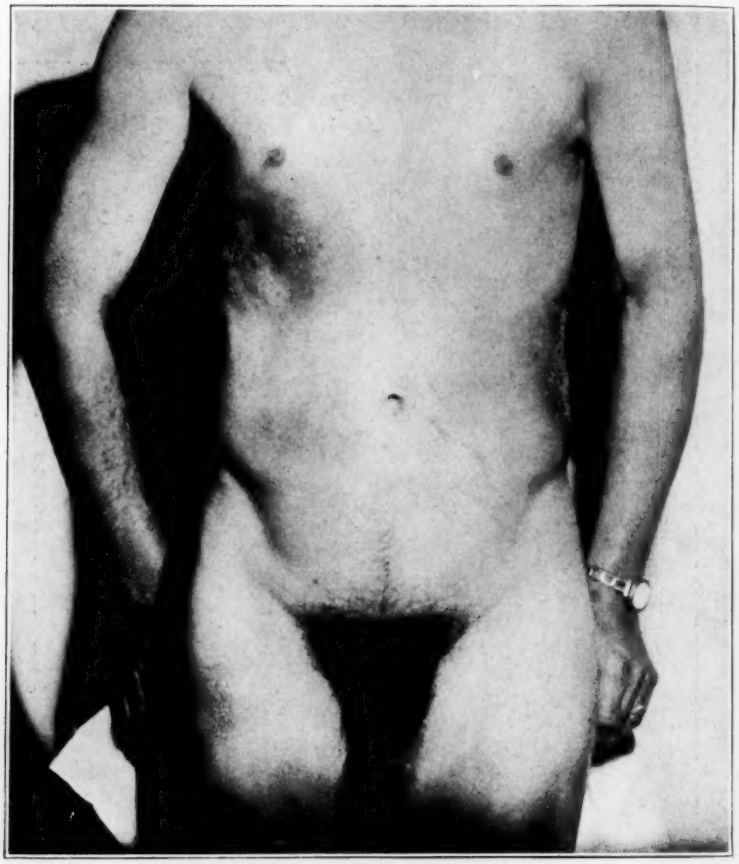

Fig. 5.—Photomicrograph of the infiltrate seen in figure 4, showing the character of the infiltration: largely lymphocytes, some connective tissue cells and an occasional mast cell and plasma cell. Magnified 950 diameters.

corneum, too, was normal, aside from the fact that in localized areas there was parakeratosis with areas of superficial micro-abscess formation. There was slight vacuolar degeneration in the epidermis, particularly in the lower half; there was a mild blending of the basal layer with the underlying cell infiltration.

A dense, diffuse cellular infiltration had involved the papillary layer of the corium and the upper third of the reticular layer of the corium, which was com-

posed largely of lymphocytes, but partially, also, of connective tissue cells, with an occasional chromatophore, mast cell and plasma cell and an occasional cell difficult to classify. There was practically no cell detritus. The lower two thirds of the corium showed a patchy, perivascular, cellular reaction similar in all essentials to the dense, diffuse infiltration above. In this infiltrate the elastic tissue was completely destroyed.

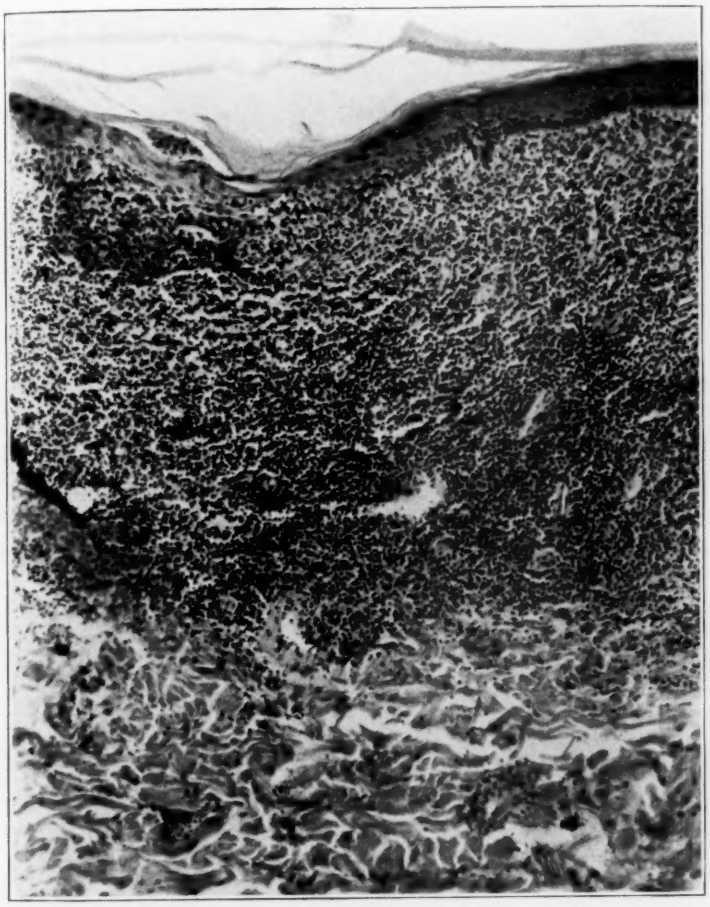

Fig. 6.—Photograph of the patient taken in August 1934, two and one-half years after the first visit, showing enlargement of the patches, especially of the one on the left side.

Subsequent Course.—The patient was shown at a meeting of the Chicago Dermatological Society on Feb. 15, 1933, as having idiopathic atrophy of the skin with poikiloderma-like changes.

In the discussion that followed Dr. Ormsby stated that in the original case reported by Dr. John E. Lane and himself the eruption looked much like this one,

except that there were more atrophy and more telangiectasia and that the condition in his case more closely resembled healed radiodermatitis.

Dr. Senear and Dr. Finnerud thought that the condition resembled poikiloderma in many respects, but the vegetative growths on the large patch suggested to them that it might be mycosis fungoides in the premycotic stage.

The patient was later shown at the clinical meeting of the American Dermatological Association in June 1933 and later at the Dermatological Conference of the Mississippi Valley in January 1934. At that time there were perceptible changes. The vegetative crusts on the patches on both flanks were much more evident. The patches were larger, and the skin, while nonpruritic, was drier and

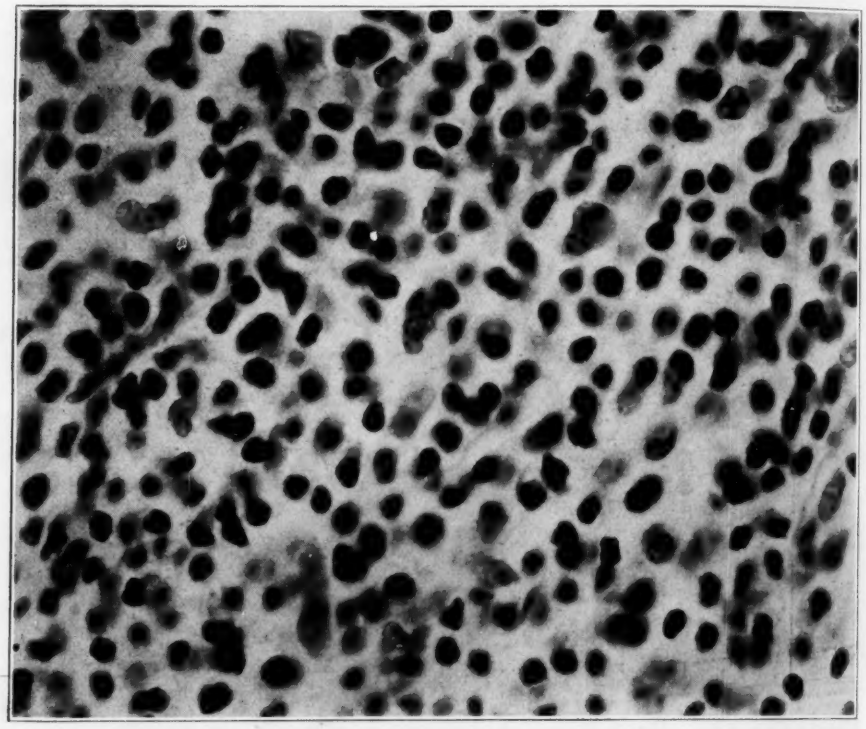

Fig. 7.—Appearance of the front of the trunk at time of the patient's last visit.

more annoying. On January 20, the day of the meeting, the erythrocyte count was 5,300,000; the leukocyte count, 9,100, and the hemoglobin content, 92 per cent. The differential count showed small mononuclears, 16 per cent; monocytes, 15 per cent; polymorphonuclears, 68 per cent, and eosinophils, 1 per cent. The erythrocytes were of good color and of normal size and shape.

In the discussion following this presentation Dr. Wile offered a diganosis of mycosis fungoides, in spite of the fact that many of the lesions showed atrophy and there was no pruritus. Dr. Weiss of St. Louis also offered that diagnosis.

After this meeting the patient, who lived at a considerable distance, went home and was not seen again until August 1, when he went to St. Luke's Hospital for a week's study of his condition.

The patches on the flanks, especially those on the left one, had grown considerably, and the vegetative crusts were more annoying. There were two glandular enlargements in the wall of the chest just below the right axilla. These were surgically removed and cultured, and guinea-pigs were inoculated with some of the glandular material. The cultures were negative for tubercle bacilli, and the inoculations had apparently no effect on the guinea-pigs.

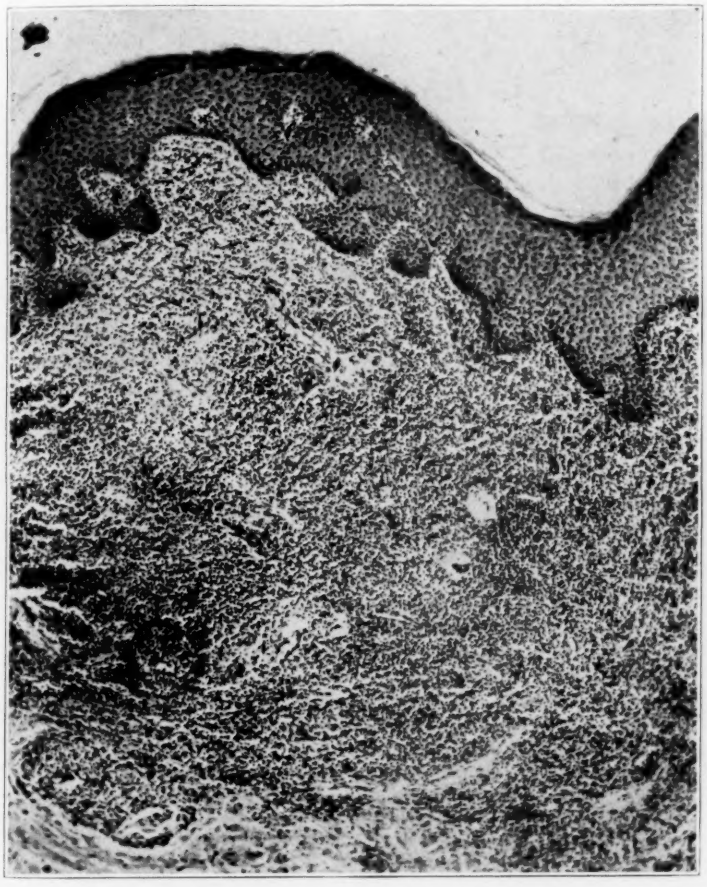

Fig. 8.—Photomicrograph of the second section, taken two and one-half years after the first section, showing acanthosis of the epidermis and dense cellular infiltration in the corium. Magnified 70 diameters.

The patient was now 44 years old; his pulse rate was 80, and his blood pressure, 112 systolic and 70 diastolic. Most of the cutaneous lesions showed considerable atrophy, with wrinkling and loss of elasticity. The basal metabolic rate was again normal. The sugar tolerance reaction and the blood chemistry were normal. Examination of the blood showed 4,820,000 red cells, 8,750 white cells, 95 per cent hemoglobin, 36 per cent small lymphocytes, 2 per cent monocytes, 58 per cent polymorphonuclears, 3 per cent eosinophils and 1 per cent basophils.

Second Histologic Examination.—Another piece of tissue was excised from one of the vegtative growths on the left flank, and this was examined microscopically. The epidermis showed alternating areas of atrophy and acanthosis. The basal layer in most places was sharply differentiated from the underlying cellular infiltration. Otherwise, there were no noteworthy differences between it and the epidermis in the section already described.

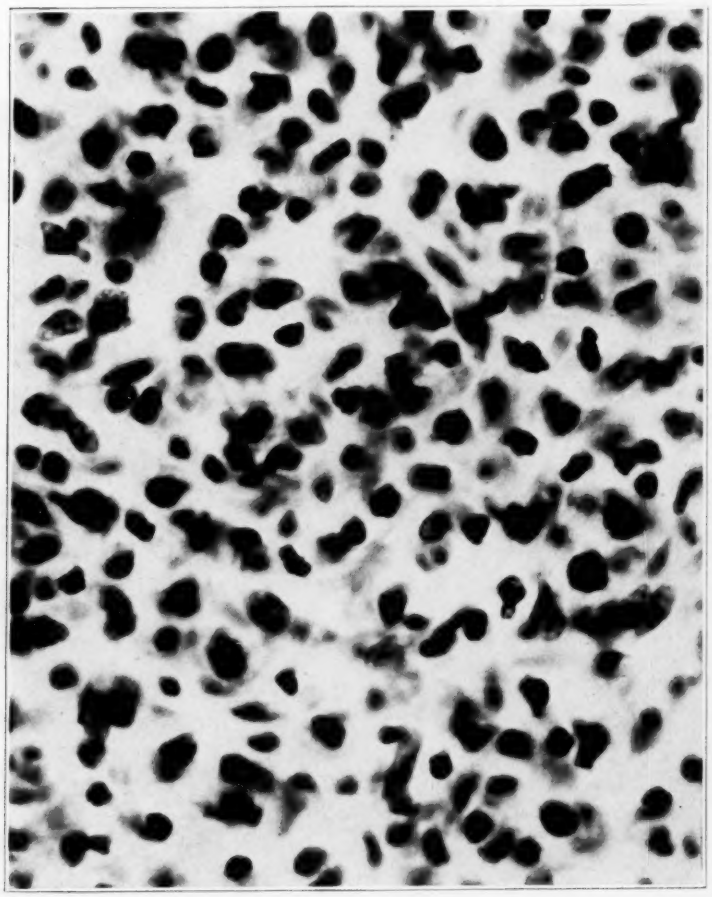

Fig. 9.—Photomicrograph showing the multiplicity of cell types of the infiltration seen in figure 8. Magnified 950 diameters.

There was a dense, diffuse cellular infiltration involving the papillary layer and the upper half of the reticular layer of the corium, in which the elastic fibers were completely destroyed. This infiltrate was composed largely of lymphocytes, but with a much more striking multiplicity of cell types than in the section studied in 1932.

Many of the cells were very irregular in shape and size. An occasional one was stellate, semilunar or comma-shaped. A number were difficult to classify

definitely. This infiltrate was laid down in a rather delicate reticulum. Eosinophils were much more in evidence than they were in the section studied two years before. The area of cellular infiltration was rather rich in blood vessels, and the infiltrate in the lower half of the corium, though dense, was largely perivascular and periglandular. It even extended in a mild degree into the hypoderm.

One of the two excised lymph glands submitted for examination measured 1.8 by 1.2 cm. On the surface made by cutting there was a soft, gray-red tissue, with some portions grayer and more contrasting. Histologic examination revealed hyperplasia of the lymphoid tissues and lymph node structures. The tissue pattern showed no characteristic changes. There were many solitary nodules with conspicuous germinal centers. The sinusoids were large, and there was hyperplasia of the lining cells.

REVIEW OF THE LITERATURE

Ever since 1906, when Jacobi presented an unusual case of a condition which he termed poikiloderma atrophicans vasculare, before the Ninth International Congress of Dermatology at Bern, there has been controversy as to how to classify this disease. Jacobi's case was that of a farmer, 30 years of age. The disease had begun seven years before, with swelling of the eyelids, intense itching and a cutaneous eruption which involved the entire trunk and extremities. He had been treated four years before for pains in the joints and fatigue. These symptoms were still present. At that time he had edema of the face, which was bluish red; this condition was diagnosed as scleroderma.

There were also superficial redness of the legs and isolated scarlike changes in the skin from scratching. Jacobi reported the case more fully two years later, in 1908. The scalp was then scaly and showed atrophic spots the size of a lentil, surrounded by a hyperemic, pigmented network. The auricles were atrophic, tense and shiny. The face was bluish red to bronze and slightly puffy. The lower lids were edematous. The neck was red and was studded with telangiectases and partially covered with adherent scales. The back and chest showed widespread atrophic changes, atrophic spots of various sizes surrounded by dark pigmentation and partly by bright red to livid marbling, with numerous telangiectases and capillary hemorrhages. The hair follicles appeared as sharply limited reddish-brown spots the size of pinheads. The appearance was much like that after an extensive roentgen ray burn. The skin of the trunk was tense, thin and parchment-like but freely movable and not sclerosed. The thighs were more deeply pigmented but otherwise of similar appearance. The legs were livid, without distinct atrophy. On the arms and hands were atrophic, hyperemic and cyanotic spots. There was hypertrichosis of both forearms. On the mucous membranes of each cheek there was a delicate whitish meshed spot the size of a mark. Itching in the lesions was intense, especially at night.

Microscopic examination of a piece of involved tissue disclosed infiltration of small cells around the vessels and glands. In the older lesions

there was atrophy of all the layers of the skin, with rarefaction or disappearance of fatty tissue, atrophy and destruction of elastic tissue and alternating increase and absence of pigment.

This case was discussed freely, and Jacobi added that its closest analog was a case of Petges and Cléjat of the Dubreuilh Clinic, in which the condition was described as sclerotic atrophy of the skin, with general myositis. Jacobi believed, however, that the patient of Petges and Cléjat showed several differences from his own. From the mottled condition of the skin and its close resemblance to chronic radiodermatitis, he called the condition poikiloderma atrophicans vasculare.

In the discussion that followed this first presentation Ehrmann compared the eruption with scleroderma, Jadassohn considered it scleroderma of the most pronounced type, Kreibich regarded it as erythema which at its height might become erythematous lupus and Arndt also considered it lupus erythematosus. In closing, Jacobi still maintained that it was a disease sui generis and bestowed on it its present name.

The first case in the American literature was reported in June 1921 by John Lane, and with it was reported the case of a patient of Ormsby's who had been shown before the Chicago Dermatological Society in 1916. Lane's case occurred in a white man, 30 years of age, a chauffeur. The dermatosis in this case began twelve years previously on the back of the right thigh. Covering a large portion of the rest of the body was an almost symmetrically distributed eruption presenting many different appearances, in which the most striking features were telangiectasia, minute petechial hemorrhages, pigmentation, atrophy and ulceration. Both arms were markedly affected, the left less than the right. The mediothoracic regions, both front and back, were not much affected; the rest of the chest was, however. The buttocks and legs were covered with the eruption. This patient disappeared from observation and was not seen until February 1921, when the process had progressed still further. He was next seen in April 1922, and again in September 1922, when he was quite ill. He died on September 18. The autopsy revealed as causes of death: (*a*) Hodgkin's disease, with involvement of the lymphatic glands, pleura, muscles, subcutaneous tissue and skin, and (*b*) cellulitis of the right thoracic wall and bronchium and fibrinous pleurisy with effusion, with subsidiary poikiloderma atrophicans vasculare.

Ormsby's patient was a man of 33 years, who consulted him regarding an indurated lesion on the penis, which subsequently proved to be a lymphosarcoma, which became generalized by metastatic involvement of the abdominal and thoracic regions and terminated fatally in one year. The cutaneous eruption, detected when he first sought medical advice for the penile lesion, involved the trunk, which was covered with pigmented macules varying in size from that of a pea to that of a half-dollar, which were contiguous, producing a mottled effect. The areas

most affected were those around the waist-line, under the belt. Both arms and both legs were similarly affected, but the lesions were less pigmented. On the thighs were large areas of telangiectasia and atrophy, strongly resembling healed radiodermatitis.

Previous to the publication of Lane's paper little had been heard of poikiloderma in America. Since then interest here has increased to such an extent that a review of society proceedings reveals a large number of cases in which the patients were shown, possibly because the diagnosis of poikiloderma had been suggested by the presenter, generally merely to bring the subject up for discussion. The only other papers on the subject in the American literature have been written by Bowman and Clark, Taussig and Usher.

It is now thirty years since Jacobi first demonstrated his case of poikiloderma atrophicans vasculare and gave it that name. Yet, as I stated at the outset, there is no unanimity of opinion as to its place. Many competent dermatologists firmly believe that it is a disease sui generis. An equally qualified group hold that it is not.

Jordan, of Moscow, has written an especially interesting paper entitled "Is Poikiloderma Atrophicans Vasculare (Jacobi) a Disease Entity?" He emphasized the symptoms that one should look for, laying especial emphasis on a bright red marbling of the skin; telangiectasia; atrophy, especially in localized processes on the head and trunk; adherent scaling, and the strong resemblance of the patches to roentgen ray dermatitis. Jacobi proposed the name poikiloderma atrophicans vasculare because of the extraordinary abundance of cutaneous symptoms and the prevalent atrophy which comes about through involvement of blood vessels. This emphasis easily gave rise to misconceptions, stated Jordan, since Jacobi declared the condition in his case similar to, if not identical with, that in the case of Petges and Cléjat, although the latter case was published by both authors as one of sclerose atrophy and generalized myositis. Several later observers have described such cases as instances of poikiloderma, thereby further confusing the situation. In Jordan's opinion a number of conditions have been mistakenly reported as poikiloderma; still, he stated, there is a whole series of conditions exactly corresponding to the classic Jacobi type, which seems to exist, and alongside it are such complications enlarging the original disease picture as muscle atrophy or scaly transitions to other dermatoses, such as idiopathic atrophy, scleroderma and lupus erythematosus.

Richter, too, affirmed that poikiloderma atrophicans vasculare is an independent disease. Neither in its history nor in its clinical picture is there anything to suggest its identity with another known disease. Poikiloderma atrophicans vasculare, stated Richter, must be recognized as an independent disease, though other diseases, such as lupus erythematosus, purpura annularis telangiectodes, atrophia cutis idiopathica, para-

keratosis variegata and roentgen ray burns, may in certain stages present the same phenomena. Illustrating this same line of thought, Geiger and Konrad in reporting a case have written a paper with a title similar to that of Jordan's "Is Poikiloderma Atrophicans Vasculare an Independent Disease?" Having reported two cases prior to this one, they stated that they believed in the individuality of the disease, though they did not offer a great deal of evidence to support their views. They asserted, however, that too many conditions have been reported as poikiloderma which are not that disease. Because lupus erythematosus, scleroderma, dermatomyositis and parapsoriasis may at times show some of the symptoms of poikiloderma, they stated that there is no reason for grouping them under that title.

Fröhlich, in reporting two cases, in which he believed the etiology was definitely related to some disturbance in the endocrine system, admitted that the condition showed some similarity to other conditions of suspected endocrine origin, for example, scleroderma; he stated the belief that poikiloderma is an entity in itself, the etiology of which is probably concerned with an upset endocrine balance.

On the other hand, though Jaffé expressed the opinion that it is difficult to class poikiloderma as a disease entity, since scleropoikiloderma, scleroderma and acrodermatitis chronica atrophicans were seen coexisting in his own two cases reported as instances of scleropoikiloderma, he asserted that he was willing to consider it a separate disease, probably of endocrine origin. Here he exhibited what Jordan said to be a misconception: the inclusion of such cases as Jaffé's and one of Gluck's with cases of true poikiloderma. This misconception has grown out of Jacobi's own admission that he considered the condition in his cases similar to, if not identical with, that reported by Petges and Cléjat, although their case was reported under the name sclerosed atrophy and generalized myositis, with the sclerosis constituting an important symptom.

Examples continuing this misconception are seen in Gluck's case, in which the disease began at the age of 7 years, with muscular weakness. In the twentieth year symptoms like those of Jacobi's disease made their appearance, but the condition finally became generalized calcinosis and was later described by Lenczyk as deposits of calcium phosphate and calcium carbonate in the skin and finger-tips. In Rattman's case, described as one of poikiloderma, in which the condition had been treated as sclerodactylia, Raynaud's disease and calcinosis, and in Nagele's case, that of a girl 9 years old with enlarged blood vessels in whom nodules and an eruption resembling lichen planus developed, Jordan stated the belief that the same diagnostic mistake had been made.

Bettmann, however, stated the belief that the characteristics of poikiloderma atrophicans vasculare as pointed out by Jacobi were not

made sufficiently clear. All these cases evidently differ much in the clinical manifestations, yet all belong together. The disease, he thinks, may show more intensive changes or more diffuse development than has heretofore made itself manifest. He does not believe poikiloderma to be a form of either lupus erythematosus or scleroderma. In many cases the disease has been ascribed to hereditary causes and this explanation used to clear up unusual manifestations. This, he believes, has been overdone. To him, however, the disease is a true clinical entity, even though in many of the reported cases the condition differs considerably from Jacobi's original description.

When one consults the French literature still another point of view is evident. Opinion among the French dermatologists is divided, but they are by no means satisfied that poikiloderma is a disease sui generis.

Gougerot and Burnier recently reported an interesting case. The patient, a woman 40 years old, was first seen in 1925. Since the age of 18 the skin had been the seat of a plaquelike eruption, which covered the greater part of the body but not the face and extremities. These plaques were brownish red and covered with fine furfuraceous scales, easily removable and revealing a smooth glistening surface below without hemorrhage. When the patient was first seen a diagnosis of parapsoriasis en plaques was made.

The patient was treated with ultraviolet rays and heliotherapy. She disappeared from observation and was not seen again until 1929. At that time the eruption appeared more intense and more extensive. The upper and lower extremities were involved in an extensive network, and the pigmentation covered most of the thorax and abdomen. There were also large areas of reticular pigmentation on the neck, breasts, axillae and thighs, with a punctate atrophy in places. Scattered unequally about in the same areas occupied by the plaques of parapsoriasis were areas of telangiectasia. The lesions were not pruritic, but the picture had so changed that a diagnosis of poikiloderma was made.

The patient again disappeared from observation and was not seen for five years, until June 6, 1934. The picture had changed. There was considerable extension of the process. The face was involved. The reddish-brown patches had become very scaly, and there was a large nodular area on the back, infiltrated and painful to the touch. Its appearance was suggestive of mycosis fungoides. Histologic examination of this lesion confirmed the diagnosis.

The authors' comments are interesting. From a study of a number of cases they arrived at the conclusion that certain cases of parapsoriasis en plaque and certain cases of pityriasis lichenoides chronica should not be confused with those of poikiloderma. These diseases are two varieties of the same process. Depending on the primary predominating lesion, if large erythematosquamous lesions exist, the condition is called

parapsoriasis en plaques; if the lesions are small lichenoid papules, it is called lichenoid parapsoriasis; if small red papules are present with a motley of colors, pigmentation and atrophy, the disease is poikiloderma.

Gougerot and Burnier thus believe that poikiloderma is a malady or morbid entity due to an unknown cause; this cause may provoke not only the complete picture of poikiloderma of Petges and Cléjat and of Jacobi but also incomplete and atypical forms having the appearances of parapsoriasis en plaques and parapsoriasis lichenoides. Though Brocq has repeatedly emphasized that the small papule is the primitive lesion of parapsoriasis, Gougerot, Eliascheff and Latte also emphasized that the initial or elementary lesion of poikiloderma is a small papule, from 1 to 2 mm. in width, slightly scaling, more or less shining, lichenoid and rose red. These papules are numerous and either remain isolated or assume a retiform configuration. It is this small papule that produces the other lesions, atrophy, telangiectasia and pigmentation.

In commenting on their case and on the apparent connection of parapsoriasis, poikiloderma and mycosis fungoides, Gougerot and Burnier stated: "The problem is difficult to solve. There exists no differential sign by which it is possible to differentiate parakeratosis variegata and mycosis fungoides. Many cases presented at society meetings as cases of parapsoriasis have been later recognized as mycosis fungoides."

Civatte at one time had under his care a patient with a condition diagnosed by Brocq as parapsoriasis and by Swiss dermatologists as poikiloderma, who died of mycosis fungoides. They wondered whether the two diseases, poikiloderma and parapsoriasis, constitute two initial aspects of a single morbid entity with mycosis fungoides as the terminal stage, or whether it is possible for mycosis fungoides to superimpose itself on the preceding lesions, in the same way that epithelioma engrafts itself frequently on leukoplakia and erythroplasia. Before coming to any such decision, however, they believed it necessary to accumulate more data than have been uncovered so far.

At the Lyons Dermatological Reunion, on March 21, 1929, Gaté and Michel presented a patient as having atypical poikiloderma: erythemato-atrophic dermatosis with pigmentation. On May 26, the patient was presented at the Strasbourg Reunion after the authors had made a complete histologic study of the cutaneous lesions. He was a man, 38 years old. The dermatosis began insidiously when he was 11 years old, on the calves of the legs. The eruption was generalized and consisted of telangiectasia, pigmentation and atrophy. Alopecia involved the left occipital region, the eyebrows and the ends of the mustache. There were ecthymatovegetating lesions on the left thigh. In these authors' opinion, the condition in many ways resembled that in the case described by Petges and Cléjat and by Jacobi. The ecthymatic ulcers on the thigh they diagnosed as ecthyma. The ulcers resisted all therapy

and became more and more vegetative. Just before the second presentation new vegetating nodosities appeared on the scalp and in the temporal region. Microscopic examination proved them to be mycosis fungoides.

This case Gaté and Michel reported as one of poikiloderma (atypical) with recent clinical development toward mycosis fungoides. From their study of the patient and from reading numerous works on poikiloderma, they have come to the conclusion that in poikiloderma they were confronting a disease little known or understood by most dermatologists. On the triple basis of the pathologic picture, etiology and clinical symptoms, they have searched in vain for a reliable criterion for poikiloderma. The histologic evidence offered by other students of this subject has not satisfied Gaté and Michel as being truly pathognomonic of the disease. Though many writers differ from this stand, they believe that on clinical grounds alone there is no definite clinical picture with which to make comparisons. After due consideration of all the facts, they confessed themselves unable to realize it as a true nosologic entity.

This is perhaps the American difficulty. Only five papers on poikiloderma exist in the medical literature of this country. Two of these were published by Lane, one by Bowman and Clark, one by Taussig and one by Usher. Yet the subject has not been without interest, as evidenced by a glance at the reported transactions of the meetings of the local dermatologic societies. In the last few years from thirty-five to forty patients have been shown as having poikiloderma, real or suspected. A cutaneous disease the major changes of which have resembled chronic roentgen ray dermatitis has always brought out considerable discussion as to whether or not it might be poikiloderma.

The case that I reported is not, of course, the first in which the condition showed considerable resemblance to poikiloderma and then proved to be something else. Lane presented a case before the New York Dermatological Society on Nov. 23, 1926. The patient, an unmarried woman, had a cutaneous eruption of six years' duration. It had gradually spread over the greater part of the body, with its most striking characteristics pigmentation, atrophy and minute hemorrhages. More scaling and less telangiectasia were present than are usually seen in poikiloderma, and a small, round, hard tumor was found on the dorsum of the left foot. Lane suggested the diagnosis of poikiloderma, but mycosis fungoides was also considered.

Several years later, Lane, in discussing Keim's paper on lymphoblastoma, said that his patient by that time had definite mycosis fungoides.

In this paper Keim reported that one of his patients, an American aged 46, presented a generalized eruption, which was most pronounced over the extremities, face, flanks and buttocks. Its most evident feature was the diffuse, underlying, rather bright erythema, interrupted

especially over the lower part of the back and over the buttocks by circumscribed areas of hyperpigmentation, which occurred in sharply circumscribed, definitely infiltrated, flattened nodules. There were six such plaquelike infiltrations, several of them crescentic or the shape of a horseshoe. The skin was unusually dry and covered with an almost imperceptible, fine, downy desquamation. There was no telangiectasia. With this exception the changes were decidedly suggestive of poikiloderma atrophicans vasculare. These infiltrated, crescentic plaques, together with the changes in color and pruritus, suggested mycosis fungoides. The permanent and progressive increase in the number of circulating lymphocytes established, however, beyond a doubt the clinical diagnosis of leukemia.

At the April 1933 meeting of the Chicago Dermatological Society and, again, before the clinical session of the American Dermatological Association, Perlstein presented a patient who possibly had poikiloderma. The eruption consisted of roughly symmetrical, round plaques varying in size from that of the palm of the hand to that of a plate. The entire trunk and the buttocks, thighs and arms were involved, with smaller scattered lesions on the forearms. During the last two months the face had become involved. The affected areas showed reticular atrophy and telangiectasia and resembled areas of roentgen ray dermatitis. The color varied from red to violet and brown. A specimen for biopsy taken from an infiltrated lesion on the back showed atrophy of the epidermis and slight edema. The upper part of the corium was edematous; there were loose mantles of round cells about the vessels, with occasional chromatophores in the papillary layer. The collagen fibers stained poorly in the upper part, and the elastic fibers were fragmented. In an atrophic lesion similar but more pronounced changes were seen. The basal layer was broken in places by the infiltrate; the elastic fibers were almost entirely absent in parts of the papillary layer.

The case was fully discussed by Drs. Ormsby, Otto Foerster, Senear, O'Leary, Ebert and Schmidt at the meeting of the Chicago Dermatological Society. The consensus was that this condition corresponded more nearly to that in the original case of poikiloderma of Jacobi than had the eruption of any other patient previously exhibited before the society. The presence, however, of superficial infiltrates of arcual character on the back and arm were of the type that one associates with mycosis fungoides. The view was expressed that the cutaneous picture called poikiloderma might well be the end-result of repeated insults to the skin from various factors.

A year and a half previously, on Oct. 21, 1931, at a meeting of the Chicago Dermatological Society, Dr. Hamilton Montgomery and Dr. Paul A. O'Leary presented a Jewish man, aged 46, who was obese, with marked enlargement of the breasts. The skin of the entire body, except

the mucous membranes, eyelids and fingers, was involved in a varying degree. There were patches of atrophy, with fine wrinkling of the skin, in addition to some lichenified plaques and areas of telangiectasia. Marked pigmentation of the skin, assuming a retiform arrangement, was noted in certain areas, between which were interspersed areas of atrophy and telangiectasia. General examination revealed the following noteworthy facts: A roentgenogram of the pituitary gland revealed a calcified pineal gland, calcification of the falx cerebri and a small area of calcification in the region of the internal carotid artery. Studies of the blood all gave normal results. The basal metabolic rate was —9. Studies of the capillaries revealed changes different from those seen in the usual vascular disturbances or in scleroderma. The patient's sweat activity was reduced, but there was no increase in temperature on hot days.

In discussing this case, Dr. Otto Foerster said:

> There are points of approach to a diagnosis in this case in the pituitary changes that are present. . . . The rapid development of a diffuse scaling process involving a large part of the cutaneous surface with subsequent atrophic changes and the development of a peculiar hyperpigmentation and punctiform telangiectasia, with areas of depigmentation, oblige us to give consideration to a diagnosis of poikiloderma atrophicans vasculare. However, many of the cases so diagnosed and recorded have been shown eventually to be variants of erythematosus lupus, perhaps atrophodermas or the end-changes in scleroderma, and some later have been proved to be mycosis fungoides.

In a case of Ormsby's the patient, a woman, when first examined the previous year, had the classic nodules and plaques of mycosis fungoides. After treatment for a year all these lesions had disappeared, and in their places were large areas of idiopathic atrophy, similar in many respects to the picture presented by this patient.

In discussing the cases of two patients with suspected poikiloderma shown at the Dermatological Conference of the Mississippi Valley in St. Louis, Wile said: "There does not seem to be a general opinion as to what constitutes poikiloderma, and there is neither a background for it nor associated observations, except for the occasional one of an abdominal neoplasm."

Goeckerman, in discussing the same cases, said that he had observed a case in Europe with Professor Jadassohn that he thought was an instance of exactly what he, himself, would call poikiloderma, on the basis of morphologic characteristics. If the characteristics are as definite as that, dermatologists are calling a number of conditions poikiloderma that do not answer Jacobi's description. I have a strong suspicion that poikiloderma may be merely a different type of some condition producing atrophy, with which dermatologists have been familiar in the past.

The classification of the types of poikiloderma most commonly adopted is: (1) poikiloderma of Civatte, (2) poikiloderma atrophicans vasculare, (3) poikilodermatomyositis (Petges and Cléjat) and (4) scleropoikiloderma.

It is no longer necessary to consider the poikiloderma of Civatte as part of this group. Civatte himself made the statement that although he had never seen any of Riehl's cases, from a study of histologic sections and a review of the literature he was forced to conclude that the poikiloderma of Civatte and Riehl's melanosis were one and the same disease.

Poikilodermatomyositis and scleropoikiloderma, according to Jordan and Midana, are types of poikiloderma in which the complications of myositis and sclerosis simply enlarge the original disease picture. This leaves the poikiloderma of Jacobi as its sole representative.

The disorder can be divided into two distinct classes, affirmed Midana: first, a group of cases in which the disorder is characterized by a purely cutaneous symptomatology (pure poikiloderma) and, second, a group in which, in addition to the cutaneous eruption, the disease can show a myosclerosing syndrome (poikilodermatomyositis). These two clinical types are not sharply distinct from one another.

Oppenheim divided poikilodermatomyositis into three main types: first, the type described by Jacobi and by Petges and Cléjat; second, a congenital type, with nevoid cutaneous changes, and, third, poikiloderma as a terminal phase of a great variety of cutaneous diseases.

The etiology of the disease is also obscure. The condition has affected females more than it has males. It occurs for the most part in the third, fourth and fifth decades of life, although in Zinsser's two cases it began in childhood following frost-bitten fingers. Many factors, such as congenital predisposition, toxic influences, atmospheric conditions and disorders of the endocrine system, have been offered to explain its pathogenicity. However, endocrine disorders have been recorded in a high percentage of the reported cases.

From a survey of most of the reported cases, one must conclude that there is still a great deal of confusion and uncertainty as to what really constitutes the disease. It would seem that poikiloderma atrophicans vasculare is a cutaneous syndrome characterized by a bright red marbling of the skin; telangiectasia; pigmentation; atrophy, especially in localized processes, on the head and trunk; adherent scaling and a strong resemblance to roentgen ray dermatitis. Jordan stated that there has been a whole series of cases in which these classic symptoms were present. Where to place the cases with symptoms of scleroderma and myositis has not been settled. Many of the most competent dermatologists in Europe have yet to agree among themselves on this point. Richter inclines to the view that the poikilodermatomyositis of Petges

and Cléjat and scleropoikiloderma are the same disease and that the different findings are explainable by the stage of development. He is one of those, however, who thinks that poikilodermatomyositis must be distinctly differentiated from poikiloderma atrophicans vasculare.

In Oppenheim's classification poikiloderma as a terminal phase of a great variety of cutaneous diseases is given as one of the three types of the disease. Richter also believes that the cutaneous picture of poikiloderma atrophicans vasculare may be present in certain stages of such diseases as idiopathic atrophy, lupus erythematosus, parakeratosis variegata, purpura annularis telangiectodes and roentgen-ray burns.

Such a point of view will explain the cutaneous picture seen in my case, in Lane's and Keim's and in those reported by Gaté and Michel and by Gougerot and Burnier. Probably if many cases in which the picture of poikiloderma is now outstanding are followed up and carefully watched, the disease will prove to be simply one phase of one of the better known chronic inflammatory dermatoses.

Mycosis fungoides, like syphilis, has always simulated other disease processes. In this instance, as in those cases recorded by Lane, by Gaté and Michel and by Gougerot and Burnier, it appears that in addition to its other and known characteristics it may simulate in many respects the picture of poikiloderma atrophicans vasculare.

SUMMARY

Among authorities there is considerable difference of opinion as to what symptoms should represent the picture of poikiloderma atrophicans vasculare.

Some authors doubt whether it is a separate disease, while others believe firmly that it is a definite clinical entity with a clearcut symptomatology.

It is not generally known that poikiloderma-like symptoms may be part of the picture of many chronic inflammatory dermatoses.

Oppenheim has divided poikiloderma into three main types: (*a*) the type described by Jacobi and by Petges and Cléjat; (*b*) the congenital type, with nevoid cutaneous changes; (*c*) poikiloderma as a terminal phase of a great variety of cutaneous diseases.

A case is reported in which the patient when first seen and examined presented many of the symptoms of poikiloderma, but examination several years later of new specimens taken for biopsy gave definite evidence that the condition was a rather unusual manifestation of mycosis fungoides. This case would seem to fit well into the third type of Oppenheim's classification

The literature on poikiloderma is reviewed, and the opinions of the various authors are recorded.

BIBLIOGRAPHY

Abramowitz: Poikiloderma Vasculare Atrophicans, Arch. Dermat. & Syph. **19**: 479 (March) 1929.

Adrian, M. C.: Bull. Soc. franç. de dermat. et syph. **35**:964, 1928.

Bagnoli, N.: Arch. ital. di dermat., sif. **9**:647, 1933.

Bechet, Paul E.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **29**:462 (March) 1934.

Bettmann: Arch. f. Dermat. u. Syph. **129**:101, 1921.

Bowman, K. M., and Clark, E. C.: A Case of Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **15**:583 (May) 1927.

Fernet, Mornet and Odinet: Bull. Soc. franç. de dermat. et syph. **38**:1438, 1931.

Fröhlich, H.: Arch. f. Dermat. u. Syph. **163**:437, 1931.

Fuhs, H.: Arch. f. Dermat. u. Syph. **168**:505, 1933.

Gaté, J., and Michel, P.: Bull. Soc. franç. de dermat. et syph. **36**:839, 1929.

Geiger and Konrad: Arch. f. Dermat. u. Syph. **164**:189, 1931.

Gougerot and Burnier: Bull. Soc. franç. de dermat. et syph. **41**:1528, 1934.

——Eliascheff and Lotte: Bull. Soc. franç. de dermat. et syph. **35**:806 (Nov.) 1928.

Gross: Poikiloderma-Like Changes of the Skin, Arch. Dermat. & Syph. **21**:480 (March) 1930.

Jacobi, E.: Verhandl. d. deutsch. dermat. Gesellsch., 1906, p. 321.

Jaffé, K.: Arch. f. Dermat. u. Syph. **159**:257, 1930.

Jordan, A.: Dermat. Wchnschr. **89**:1829, 1929.

Keim, H. L.: The Lymphoblastomas: Their Interrelationships, Arch. Dermat. & Syph. **19**:590 (April) 1929.

Lane, J. E.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **4**:563 (Nov.) 1921; Poikiloderma, ibid. **15**:621 (May) 1927.

Montgomery, Hamilton, and O'Leary, Paul A.: Poikiloderma Atrophicans Vasculare (Jacobi)?, Arch. Dermat. & Syph. **25**:943 (May) 1932.

Oppenheim: Zentralbl. f. Haut- u. Geschlechtskr. **36**:163, 1931.

Ormsby, O. S.: J. Cutan. Dis. **35**:42, 1917; A Case for Diagnosis (Poikiloderma?), Arch. Dermat. & Syph. **18**:304 (Aug.) 1928.

Perlstein, Minnie O.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **28**:735 (Nov.) 1933.

Petges and Cléjat: Ann. de dermat. et syph. **7**:550, 1906.

Rasch, C.: Brit. J. Dermat. **37**:477, 1925.

Richter, W.: Arch. f. Dermat. u. Syph. **167**:233, 1933.

Sequeira: Brit. J. Dermat. **26**:213 and 249, 1914.

Taussig, L.: Poikiloderma Atrophicans Vasculare, Jacobi, Arch. Dermat. & Syph. **25**:882 (May) 1932.

Traub: Poikiloderma, Arch. Dermat. & Syph. **15**:728 (June) 1927.

Usher, B.: Poikiloderma Vasculare Atrophicans, Arch. Dermat. & Syph. **25**:683 (April) 1932.

Wertheimer: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **14**:594 (Nov.) 1926.

Whitehouse, H. H.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **7**:836 (June) 1923.

Wile: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **20**:540 (Sept.) 1929.

Zeisler: Poikiloderma Atrophicans Vasculare: Jacobi's Disease, Arch. Dermat. & Syph. **7**:709 (May) 1923.

Zinsser, F., in Neisser, A., and Jacobi, E.: Ikonographia dermatologica, Berlin, Urban & Schwarzenberg, 1910, vol. 5, p. 219.

ABSTRACT OF DISCUSSION

Dr. L. R. Taussig, San Francisco: Dr. Oliver has presented a complete discussion of the present status of poikiloderma atrophicans vasculare. He has stressed particularly the difference of opinion held by various dermatologists as to whether this condition is a disease sui generis or not. When I presented my paper on this subject in 1931 I was of the opinion that it was a disease entity and stated so. Since then I have become doubtful. In the first place, a rather large number of conditions which were reported on under the term poikiloderma have since been proved to be other conditions, notably, mycosis fungoides, Hodgkin's disease, lymphosarcoma, scleroderma and myositis. It is not logical to believe that one disease entity has changed to another, but it is reasonable to believe that the earlier condition was an unusual and unrecognized manifestation of the condition which developed later. In the second place, the suggested classifications indicate an unduly wide variation in symptomatology. Thus, poikilodermatomyositis has been used to include the condition described by Petges and Cléjat of myositis with poikilodermatous cutaneous changes, and scleropoikiloderma to include scleroderma and calcinosis with similar cutaneous eruptions.

The histologic picture in the case that I reported was that of a more or less reticular hyperplasia of endothelial cells lying just beneath the atrophic, flattened epidermis and pushing down or destroying the hair follicles and skin glands. This picture is that of a condition resulting from some chronic inflammatory process, and it is easy to conceive that different types of inflammation might have produced it. These considerations lead to the conclusion that poikiloderma is a symptom that may occur in a number of different, and most likely unrelated, conditions. It seems evident that poikiloderma is a symptom in Dr. Oliver's case, and not a disease. It is also evident that this statement is true for a considerable number of cases that have been presented under the title of poikiloderma atrophicans vasculare. There may be such a disease entity, but, if so, it is far more rare than the literature would indicate.

Dr. Oliver S. Ormsby, Chicago: I agree with Dr. Oliver's findings relative to this disease and arise only to make one statement and emphasize the findings in the case of an early stage of the condition that I observed. There was no connection in that case between the lymphosarcoma and the poikiloderma. The patient consulted me on account of the lymphosarcoma. The poikiloderma was incidental and was of several years' duration, and the patient was not concerned with that. The lesion of the lymphosarcoma was situated on the glans, with extension to the inguinal glands, and later involved the mediastinal region and became generally disseminated, and this disease went on to a rapidly fatal termination. In this instance, therefore, the condition was simply an independent sarcomatous lesion developing in a patient who had long-standing poikiloderma.

Dr. Fred Wise, New York: It is unfortunate that the word poikiloderma has crept into the literature, for this reason: It is used indiscriminately, to indicate variegated lesions, instead of being limited to eruptions presenting a definite picture of poikiloderma atrophicans vasculare. There are marked differences between eruptions presenting variegated lesions and the eruption which Dr. Oliver described. In describing certain cases with variegated lesions one should employ the term "poikiloderma-like" lesions. I share with Dr. Oliver the belief that

poikiloderma atrophicans vasculare is much more rare than the reading of the transactions in the ARCHIVES OF DERMATOLOGY would lead one to believe. I believe also that every case of poikiloderma of Jacobi, if followed to the end, will demonstrate the fact that the condition is not a cutaneous disease per se but the manifestation of some grave internal disorder.

With respect to the case that Dr. Oliver described, I have the impression that the condition was mycosis fungoides from its inception and that the poikiloderma-like changes were manifestations of the same disease. I do not believe that Dr. Oliver's case is comparable to the original picture described in the "Ikonographica dermatologica" by Jacobi. It seems to me to be most likely that sections obtained from any of the early lesions in Dr. Oliver's case would probably be interpreted as showing mycosis fungoides by the dermatopathologist; the question of a possible transmutation from one disease to another is a controversial one.

DR. E. A. OLIVER, Chicago: I am glad to know that Dr. Taussig holds practically the same views that I do in regard to poikiloderma. He has given an excellent résumé of the subject.

I am sorry that I did not make it plainer that Dr. Ormsby's patient consulted him for a lymphosarcoma of the penis and died as a result of a generalized lymphosarcomatosis. The poikilodermatous picture was only a secondary feature.

The object of this paper was to point out the fact that poikilodermatous changes may be part of the picture of many chronic inflammatory dermatoses. There may be and possibly is a true poikiloderma atrophicans vasculare. If there is, few if any, dermatologists have seen it. In a case presented by Dr. Perlstein at a meeting of the Chicago Dermatological Society as a possible case of poikiloderma, all who saw the patient, and that included Dr. Otto H. Foerster and Dr. Ormsby, agreed that the disorder was as nearly like that described by Jacobi as that in any case ever presented before the society. Yet Dr. Otto Foerster called attention to the fact that there were numerous arciform infiltrations present that made him believe that the patient might succumb to mycosis fungoides.

In many of the cases presented as possible cases of poikiloderma the possibility that mycosis fungoides might ultimately develop was brought out in the discussion.

I believe that dermatologists must revise somewhat their previously accepted ideas of this disease and accept Oppenheim's classification as the best one.

DIRECT MICROSCOPIC EXAMINATION OF THE SKIN

A METHOD FOR THE DETERMINATION OF THE PRESENCE OF FUNGI

J. H. SWARTZ, M.D.
BOSTON
AND
NORMAN F. CONANT, PH.D.
DURHAM, N. C.

A simple method by which cutaneous scales may be examined microscopically and the presence or absence of fungi determined with accuracy has long been sought by the clinician. At the present time the use of clearing agents, such as potassium hydroxide, sodium hydroxide, xylene, chloral hydrate and glycerine, while permitting a microscopic examination of the scales, has led in many instances to a positive diagnosis of fungous infection because of the presence of artefacts which may easily be interpreted as fungi. To avoid this difficulty we searched for a stain which would select and differentiate the hyphae and spores of fungi from the various artefacts and the surrounding epidermal cells. The technic which was finally worked out and the results obtained are presented in this paper.

ARTEFACTS WHICH SIMULATE FUNGI

The chief artefacts which simulate fungi so closely as to demand an unusual degree of caution on the part of an examiner are crystals, fat globules and the "mosaic fungus." It may be well to consider these before presenting a technic which eliminates them from preparations for microscopic examination.

Of the artefacts listed the most misleading is the mosaic fungus, but there are others which have caused confusion. For example, imperfections in cover slips are often encountered, and because of the linear, radiating, occasionally branching appearance of the markings on the glass, these figures have been confused with fungi. These figures, however, are not the result of any method used in preparing the scales for examination and do not appear in the skin proper but are seen in a plane sufficiently above it to arouse the suspicion of the observer. By careful focusing, therefore, this type of artefact may be readily recognized.

From the Department of Cryptogamic Botany, Harvard University.

Read at the Fifty-Eighth Annual Meeting of the American Dermatological Association, Inc., White Sulphur Springs, W. Va., May 2, 1935.

The most confusing artefacts, however, are those which appear in the scales as a result of the type of clearing agent used. Of these, potassium hydroxide is the most effective and has, therefore, been used most extensively. Yet, although effective, potassium hydroxide presents certain disadvantages, in that it results in the formation of crystals, which at times are present as isolated, elongated, anastomosing hypha-like growths with sporelike particles, giving an appearance not unlike that of actual fungi. Despite these resemblances, however, they can be distinguished from true fungi by a lack of uniformity, a lack of content and an irregularity of outline where elongated appearances are assumed. By flooding the preparation with additional potassium hydroxide these formations are lost, whereas true fungi remain visible.

The use of potassium hydroxide has also been responsible for another type of artefact, namely, fat globules. These particles of fat when acted on by potassium hydroxide may at times assume the contour of spore forms and in some preparations even simulate budding. If the globules are extended, their parallel-walled appearance easily permits their interpretation as true fungous elements. The rounded globules may be distinguished from actual fungous spores or yeastlike cells, however, by the lack of content and extreme variability in size, while the elongated types lack the regularity of septation found in the hyphae of the true fungi. Moreover, this type of artefact may be eliminated to a certain extent by first immersing the scales in ether and then mounting them in potassium hydroxide. This procedure eliminates much of the fat, and the danger of confusing globules with fungous spores is greatly lessened.

The foregoing artefacts are not the most troublesome, however. The artefact which has caused the most confusion, and about which there is still a great deal of controversy, is the so-called mosaic fungus. Its intercellular netlike, anastomosing appearance in scales has readily led to its interpretation as a true fungus. By some, a discussion of this peculiar intercellular material may be regarded as needless. The subject, however, can hardly be considered a closed book when the literature concerning it covers a period from 1888 to the present time and a diversity of opinion still exists as to whether it is a product of inflammatory tissue, keratohyalin, fat, a free fatty acid, soap, a degenerate fungus or a true normal fungus. A book to be permanently closed should be thoroughly understood.

The mosaic formation was presented to us forcibly when we examined many preparations of scales, and it was only after comparing the reactions of this substance and those of hyphae of normal fungi to certain reagents that we were convinced of the nonfungous nature of this intercellular material. It is pertinent, in order to appreciate this difficulty, to review the situation as it has developed in the literature.

THE MOSAIC FUNGUS

One of the first comprehensive works on the examination of scales from the skin may be said to be that of Ries.[1] When examining scales from psoriasis for the "epidermidophyton" [sic.], reported on earlier by Lang,[2] he was able to demonstrate the presence of certain sporelike bodies in scales which had been cleared in a solution of 6 per cent potassium hydroxide as Lang had recommended. After the preparations had stood for twenty-four hours, he noted that these bodies grew larger and that the intercellular spaces became filled with elongated strands of material similar to mycelial elements. He characterized this condition when he wrote: "The space can be so broad that the cells which are now often light and not granulated seem bedded into a mosaic in this shining mass." He likened the material thus formed to fungous threads.

Because he found the so-called epidermidophyton in such profusion, however, he extended his studies to include cutaneous conditions other than psoriasis. In these studies he examined skin involved by prurigo, general ichthyosis, lichen pilaris, lupus erythematosus, eczema seborrhoeicum, alopecia pityroides and comedones. Preparations of skin presenting each of these conditions contained the epidermidophyton seen in the scales from psoriasis. Ries was able to find these elements not only in skin showing a definite diseased condition, but also in healthy skin. During further treatment of scales with various reagents and stains, Ries came to the conclusion that the elements had nothing to do with psoriasis and were, indeed, not fungi. He discussed the possibility of their being fat or hyalin and came to the conclusion that they were the latter.

At a much later date, Weidman [3] referred to this mosaic appearance in scales treated with potassium hydroxide. By dissecting out the substance between the cells he proved that the intercellular network was not due to air spaces, and he expressed the belief that the material was degenerate fungus, if, indeed, it was of fungous nature.

Likewise Becker and Muir [4] were able to demonstrate "a large amount of fungus-like material" in scales from tinea amiantacea, but considered this substance to be the result of epidermal inflammation.

---

1. Ries, E.: Die pathologische Anatomie der Psoriasis, Vrtljschr. f. Dermat. u. Syph. **20**:871, 1888.

2. Lang, E.: Vorläufige Mittheilung von einem neuen Untersuchunsergebnisse bei Psoriasis, Vrtljschr. f. Dermat. u. Syph. **11**:257, 1879.

3. Weidman, F. D.: Laboratory Aspects of Epidermophytosis, Arch. Dermat. & Syph. **15**:415 (April) 1927.

4. Becker, S. W., and Muir, K. B.: Tinea Amiantacea, Arch. Dermat. & Syph. **20**:45 (July) 1929.

This decision was based on unpublished work by Becker and Ritchie,[5] who showed later that this fungus-like material could be removed by progressive treatment of the scales with absolute alcohol, ether, absolute alcohol and then 95 per cent alcohol.

In many cases investigators have noticed confusing preparations in which not only definite mycelium could be seen but also a mosaic formation. Greenwood and Rockwood,[6] for example, reported that the mosaic growth could be shown to be a continuation of the normal fungous hyphae and because of this concluded that the intercellular material represented a degenerate form of mycelium.

Griff and Itkin [7] also expressed the opinion that this intercellular material was fungous, even though its position, its irregular outline and its lack of uniform diameter were in contrast to normal mycelium.

Another report of the mosaic growth as a fungus was that of MacKee and Lewis.[8] In their work they balanced the evidence for the mosaic formation as an artefact, more especially as the result of the action of alkali on fats, against that evidence which would establish it as a fungus. They came to the conclusion that it was degenerated fungous mycelium resulting from immunity reactions instituted by the host.

In two papers by Cremer [9] and Stumpf,[10] the most recent on the subject, the mosaic growth is considered to be inert intercellular material and not fungus. Cremer was inclined to agree with Becker and Ritchie [5] in their conclusion that the substance confined between the cells was organic material and the result of epidermal inflammation. Stumpf, however, believed the mosaic formation to be a free fatty acid because he was able to stain it. He was able to demonstrate the difference between true fungus and the mosaic formation by the use of various clearing agents. He found that potassium hydroxide brought out both entities equally, as did sodium hypochlorite, but xylene, which does not saponify fats, did the same, while methyl salicylate brought out the actual fungus but showed no trace of the mosaic growth. He also found that the mosaic growth was soluble in absolute alcohol but insoluble in

---

5. Becker, S. W., and Ritchie, E. B.: The Rôle of Yeasts in the Production of Superficial Dermatitis, Arch. Dermat. & Syph. **22**:790 (Nov.) 1930.

6. Greenwood, A. M., and Rockwood, E. M.: The Skin in Diabetic Patients, Arch. Dermat. & Syph. **21**:96 (Jan.) 1930.

7. Griff, Fanny, and Itkin, M. M.: Zur Aetiologic der Dyshidrosen, Acta dermat.-venereol. **11**:508 (Dec.) 1930.

8. MacKee, George M., and Lewis, George M.: Keratolysis Exfoliativa and the Mosaic Fungus, Arch. Dermat. & Syph. **23**:445 (March) 1931.

9. Cremer, G.: Untersuchungen über die Epidermophytie der Füsse und Hände in Amsterdam, Arch. f. Dermat. u. Syph. **169**:244, 1933.

10. Stumpf, Walther: Uber saprophytäres Vorkommen von Hyphomyceten auf klinisch gesunder Haut unter gesonderer Berücksichtigung der Mosaic Fungi, Arch. f. Dermat. u. Syph. **170**:449, 1934.

water. In addition he was led to believe that it was not a fungus, for from the skin of fifty healthy persons in which he was able to demonstrate a mosaic formation in 97 per cent of the cases he was not able to culture a single fungous pathogen.

Since a great many investigators base a positive diagnosis of fungous infection on the appearance of a mosaic formation alone, there are many conflicting reports concerning the presence of fungi in preparations for microscopic examination. There are, then, at the present time these various artefacts which annoy investigators to the extent that only in isolated cases is the expenditure of time necessary for careful, sincere examination of skin advisable. To meet this difficulty it seemed to us that the use of some selective stain would prove the best method of establishing with certainty the presence or absence of fungi in scales.

TECHNIC FOR EXAMINING SCALES

A technic that would permit rapid examination of material and would convincingly establish the presence or absence of fungi seemed to us to be one in which a stain would be employed. With this in mind we tried several bacteriologic stains and combinations of stains, but we found that in most cases the material to be examined was too thick to permit satisfactory clearing. It was found that in order to retain a stain through the alcohols into balsam the skin, being thick, had to be so overstained as to prevent examination. When to avoid this light staining was used, the penetration by the stain was so slight that the stain was lost in progressive steps. It was evident, then, that a different method must be used, one that would clear the thick scales yet at the same time differentiate the fungus from the tissue.

Such a combination of clearing agent and stain, lactophenol with cotton blue, has been used by mycologists for several years. The formula for lactophenol as found in Langeron's[11] "Précis de microscopie" is as follows:

Lactic acid	1 Cc.
Phenol crystals	1 Gm.
Glycerin	2 Cc.
Water (distilled)	1 Cc.

To this may be added 0.5 per cent cotton blue (C4B Poirrier), which was considered by Langeron to be the best type.

When scales were gently heated in a drop of this liquid on a slide and a cover glass was pressed on them, it was seen that fungi, when present, stained more deeply than did the epidermal cells. The varied thicknesses of the scales, however, hampered the effectiveness of the clearing action of the lactophenol, and it was found advantageous to subject the scales to preliminary clearing in a 5 per cent solution of potassium hydroxide. After this preliminary treatment the scales were transferred to a watch crystal and washed with water. When the action of the potassium hydroxide was stopped after two or three minutes of washing, the scales were gently heated in a drop of the lactophenol-cotton blue mixture, and a cover glass was pressed on the preparation. The clearing action of the

11. Langeron, M.: Précis de microscopie, Paris, Masson & Cie, 1925, pp. 542, 544, 547 and 960.

potassium hydroxide was continued by the lactophenol, and the epidermal cells received a light bluish stain, while the granular protoplasmic content of the fungus

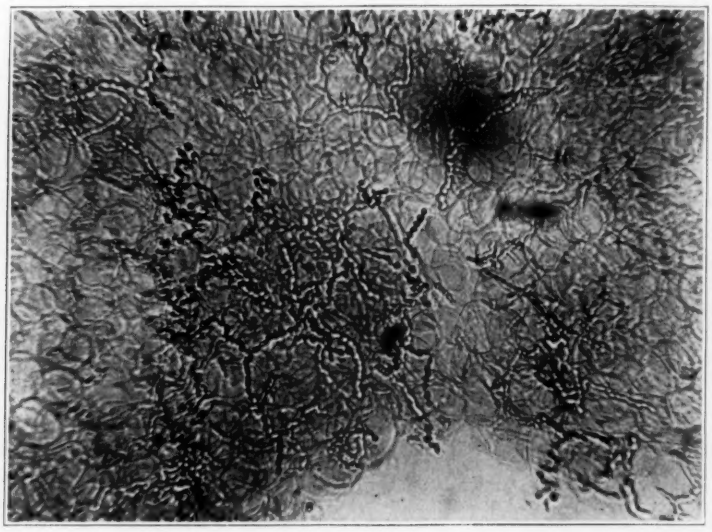

Fig. 1.—Section (× 150) showing sharp differentiation between deeply stained fungus cells and epidermal cells. No mosaic formation is present.

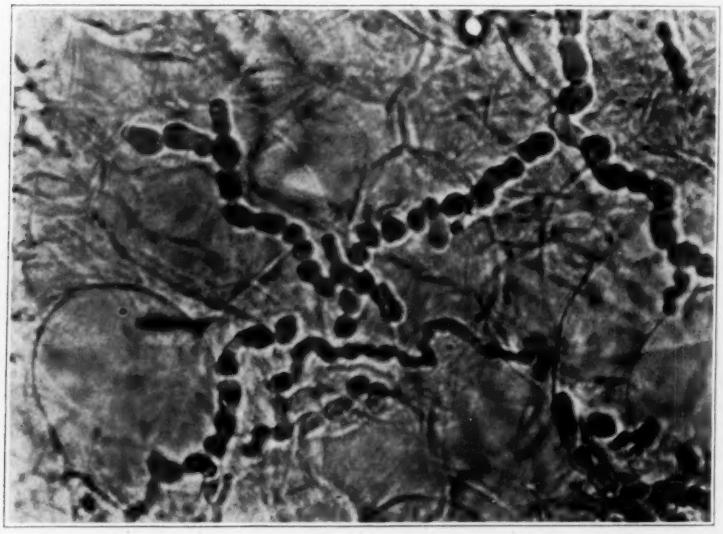

Fig. 2.—Section shown in figure 1 at a magnification of × 630.

was heavily stained (figs. 1 and 2). It was noted, however, that in some thick preparations the fungus was visible but slightly stained. These scales, after being treated in 5 per cent potassium hydroxide and washed in water, were stained with

cotton blue in 70 per cent alcohol (1 per cent solution). They were then mounted in clear lactophenol, and the preparation was pressed out under a cover glass. The fungi were heavily stained, showing the protoplasmic content and hyaline outer sheath (fig. 3).

Not only is this method valuable in the case of distinct, well defined fungous hyphae, differentiating them better than does potassium hydroxide alone, but it is especially advantageous in cases in which yeastlike budding cells appear in preparations. In such cases the use of potassium hydroxide alone (fig. 4) requires the greatest of caution, for many times fat globules also assume such forms, and a positive diagnosis must be given with certain reservations. When, however, such preparations are stained with lactophenol and cotton blue after treatment with 5 per cent potassium hydroxide the skin is sufficiently cleared and the artefacts are not present, while the stained budding yeastlike cells are easily recognized (fig. 5).

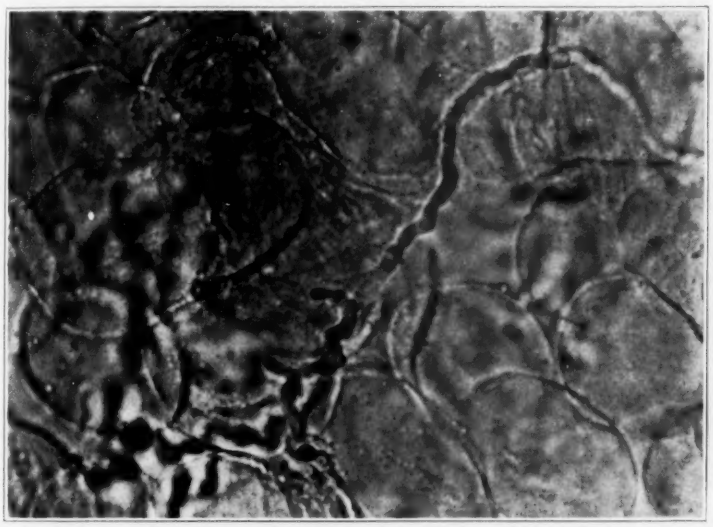

Fig. 3.—Preparation from a thick specimen showing heavily stained fungus with a clear differentiation of protoplasmic content and hyaline sheath.

Permanent preparations of stained specimens are always desirable. To obtain permanent preparations of the scales stained with lactophenol and cotton blue, all that is necessary is to wipe off the excess medium around the cover glass and cement the cover to the slide with Noyer's cement.[11] Another method of obtaining permanent preparations was found to be that of mounting the stained scale in chloral hydrate and acacia:[11]

Distilled water	50 Cc.
Chloral hydrate	50 Gm.
Glycerin	20 Cc.
Acacia	30 Gm.

The methods were found to be equally successful, but the real test, of course, is the permanence of such preparations after several years. We have not had our preparations for a sufficient time to determine their permanency, but after five months their value is unimpaired.

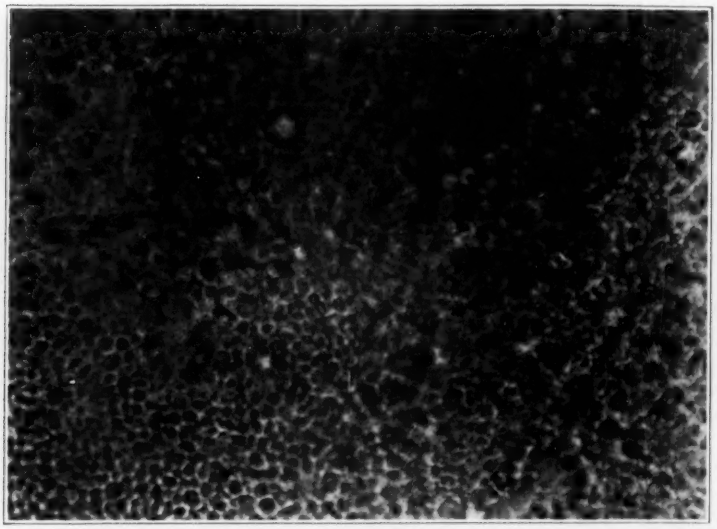

Fig. 4.—Unstained preparation showing globular formations which may be budding yeastlike fungi or fat globules.

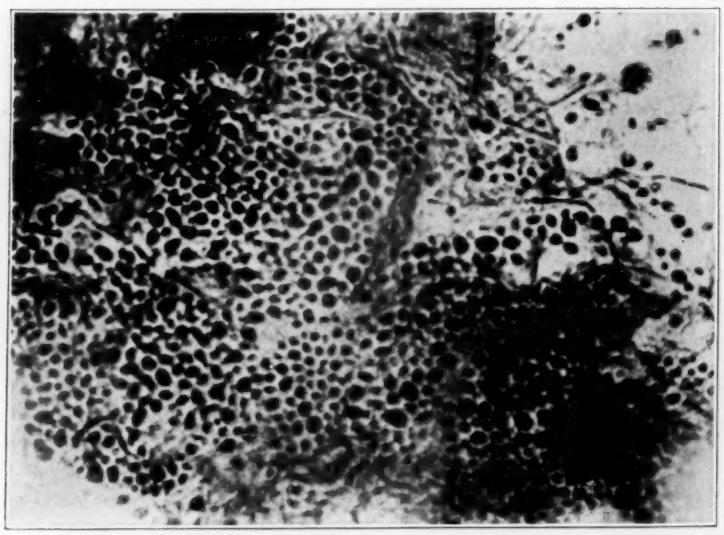

Fig. 5.—Stained preparation showing clear differentiation of yeastlike cells.

CONSIDERATION OF THE MOSAIC GROWTH

While preparing scales for staining, by first treating them in a 5 per cent solution of potassium hydroxide, there was seen a great deal of mosaic material as well as normal mycelium. It was felt that this material, if fungus, would take the stain in the same manner as the true hyphae. After the potassium hydroxide was washed from the preparation and it was stained with lactophenol and cotton blue, only the normal hyphae were seen (fig. 1). When lactophenol without the stain was used, the normal hyphae were visible, but again the preparations lacked any of the mosaic material which was seen in those treated with potassium hydroxide. To determine whether the mosaic growth was soluble in the lactophenol or had been washed out by water, many attempts were made to wash the scales thoroughly with both hot and cold water and the mosaic material was found to be insoluble in water. This clearly showed that the lactophenol was responsible for the disappearance of the mosaic material.

This behavior of the so-called mosaic fungus in the presence of lactophenol was such a contrast to the behavior of normal mycelium that we were convinced of the nonfungous nature of this material. It can hardly be said that it is a degenerate form of mycelium due to digestion of the hyphae by immunity reactions set up by the host. If it could be explained in this fashion, we feel that some partially destroyed mycelium would be seen in preparations in which both mosaic and normal hyphae are present. An intermediate, partially digested form has never been seen, however. In all preparations in which both types occurred in the presence of potassium hydroxide, either normal mycelium with absolutely no broken, irregular, partially destroyed, fantastically shaped hyphae or that intercellular netlike, irregularly outlined material called mosaic was seen. It is hard to believe that fungi so quickly and completely degenerate as to leave no trace, even on staining, while there are still normal hyphae to be seen in the preparation. In addition mosaic growth was never found to be a continuation of the normal hyphae. In preparations in which both mosaic formations and fungi were found, the former always followed the outline of the epidermal cells, while the latter never assumed intercellular, small radiating, patchlike positions. By careful focusing the two types could always be clearly separated.

When scales containing fungi in a particularly attenuated form were stained by our method, the lack of photoplasmic content did not interfere with their visibility. The hyphal walls and septations were plainly seen, and the course of the fungi in the skin could be followed. This is probably due to the lactic acid in the medium, which has a tendency to restore, by swelling, the hyphae to their normal turgidity.

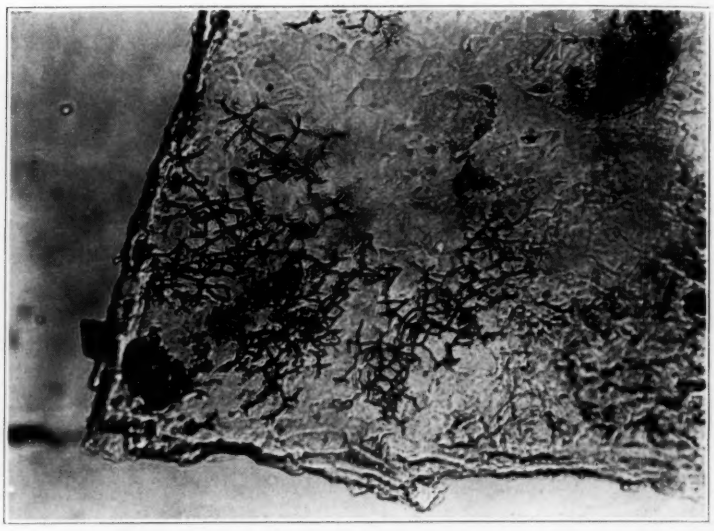

Fig. 6.—A mosaic formation in a preparation in which xylene was repeatedly renewed and allowed to evaporate.

Fig. 7.—Same formation as that in figure 6 under higher magnification.

It was thought that a change of the refractive index was responsible for the disappearance of the mosaic material when clear lactophenol was applied after treatment of the skin in potassium hydroxide. Because of this, scales were treated in potassium hydroxide and then washed in water. The mosaic formation remained visible, but it vanished when lactophenol was applied. This medium was then washed out of the preparation with water, and the mosaic growth did not appear again when bits of the skin were examined in water or potassium hydroxide. Thus, the refractive index was not a factor in its disappearance.

When it was found that the mosaic growth was soluble in lactophenol, the component parts of this medium were tested to determine what was responsible for the solubility. The mosaic material was not soluble in lactid acid, glycerin or water but was soluble in phenol, ether, 95 per cent alcohol and absolute alcohol. A microscopic examination of the scales during the application of any of these liquids was revealing in that the mosaic strands were seen to shrink, break up and finally fade out of sight. They did not appear again on the addition of potassium hydroxide.

Potassium hydroxide does not seem to be responsible for the appearance of the mosaic formation in the scales for it was seen in preparations treated with xylene (MacKee and Lewis [8]), chloral hydrate and acacia. In these preparations, however, it could be seen only faintly. When xylene, however, was repeatedly renewed after being allowed to evaporate, the mosaic formation was plainly visible (figs. 6 and 7). These figures, especially, figure 7, might lead one to believe that this material is indeed a fungus. It showed a tubular, walled structure which was not seen in preparations of mosaic growths cleared with potassium hydroxide. However, when these structures were examined for a period of time under the microscope while the xylene was allowed to evaporate, they gradually disappeared by shrinking, breaking up and fading away. Moreover, the preparation retained a faintly visible intercellular mosaic material. These could be made to appear more prominently by the addition of more xylene.

The nature of this mosaic material, other than that it is certainly not an organized fungus, is not yet wholly clear. Although the material may be fat, it could not be stained with sudan III or scarlet red or blackened with osmic acid. Ries [1] also mentioned unsuccessful attempts to stain this material with tincture of iodine, osmic acid, carmine, hematoxylin, nigrosine, Millon's reagent, chrysarobin, pyrogallol and alizarin. Stumpf,[10] however, was successful when he used Fishler's method of staining for fatty acids. When mosaic material was examined in the presence of polarized light there was no evidence of the formation of crystalloids.

SUMMARY AND CONCLUSION

The treatment of scrapings from the skin with 5 per cent potassium hydroxide, followed by washing with water and staining in lactophenol and cotton blue makes possible the easy determination of the presence of fungi. This method of preparing microscopic specimens for examination is simple in that it adds only two steps to the more common method using potassium hydroxide and is effective in that the fungi are definitely stained while the various confusing artefacts are eliminated from the picture.

This is particularly true of the mosaic growth which occurs commonly in preparations made with potassium hydroxide. This material does not seem to be the result of treatment with potassium hydroxide since it can be found in scales treated with xylene or with chloral hydrate and acacia. It was found to be soluble in ether, 95 per cent alcohol, absolute alcohol and phenol. It could not be stained with sudan III or scarlet red or blackened with osmic acid. While fungi were readily stained with lactophenol and cotton blue, mosaic material which occurred in the same preparation did not stain and was, in fact, entirely eliminated. In the presence of polarized light there was no evidence that the mosaic material was composed of crystalloid forms.

Whatever the nature of the mosaic growth we feel that we have presented sufficient proof that it is not a fungus. The staining of normal fungi in scales with lactophenol and cotton blue, the failure to find partially degenerated forms in the same preparation in which both mosaic material and fungi occurred and the failure to find morphologic connections between normal hyphae and these mosaic forms seem to disprove convincingly the theory that this material is a degenerate form of fungus.

ABSTRACT OF DISCUSSION

DR. LEE MCCARTHY, Washington, D. C.: I think Dr. Swartz is to be congratulated, as he has given something for which dermatologists have been looking for many years. How long does this examination take? Many examinations are made in the dispensary, and the physician does not have as much time as he wishes.

Another point is the length of time the specimen rests in potassium hydroxide. Sabouraud made the suggestion that passing the slide through the flame from a Bunsen burner hastens the action of the mordant. Otherwise the preparations have to lie overnight in order to clarify a specimen as thick as a piece of skin or nail.

I wish to know how this method differs from Sabouraud's method for staining hair. He used practically the same method for making permanent specimens. I made several of these over ten years ago, and they are still fairly good today. I think the method presented here is practical, and it should be excellent, particularly for the demonstration of these fungi to students in the dispensary. There is nothing the student knows less about than the demonstration of the presence of the organism causing one of the commonest skin diseases.

DR. CHARLES M. WILLIAMS, New York: Dr. Swartz sent me some slides he had prepared in this way and the demonstration of mycelia was beautiful. He sent me the formula also, but I was unable to obtain the necessary dye, and I do not know whether the one I did get will be satisfactory.

I tried this method on scales from a toe-nail that had been soaked in a 30 per cent solution of potassium hydroxide for several days and found that the difficulty then was that of washing out the potassium hydroxide. The specimen did not clear perfectly, and when the dye was added, although there was some staining at the periphery, there was cloudiness in the center. That was the fault of the technic and not of the method.

I think it is an established fact that the mosaic formation is not fungus. I have never seen a specimen in which undoubted mycelium was continuous with mosaic material. I have found both in the same specimen but never have seen one run into the other.

This method will be valuable in the cases in which one sees fragments not long enough to make the typical mosaic picture but looking something like it and also like mycelium. In my own work these have been reported as negative because I was not sure of their identity, but with this method of Dr. Swartz' I think I can tell which they are.

I wish Dr. Swartz would tell something of the method of securing this dye and the necessity of having the proper dye.

DR. JAMES H. MITCHELL, Chicago: I wish to express my appreciation of Dr. Swartz' work. At the Cleveland meeting of this association I exhibited a series of photomicrographs taken of material from a case of the Wende type of dermatitis exfoliativa. I left the preparation in place and then took pictures beginning at half an hour, one hour and on up. The mosaic formation disappeared completely, whereas the fungus remained visible for several weeks. I said at that time that I thought the so-called mosaic fungus was an artefact, and I have had no occasion to change my opinion.

NOTE: Since returning home I have tried out, with variations, the technic described by Drs. Swartz and Conant, with no success whatever. I find that the tissue stain and the fungi do not stain or else the whole mass is a deep blue. After the tissue stands in the lactophenol for some time, crystals form which render the preparation of no value.

DR. GEORGE MILLER MACKEE, New York: It looks as though Dr. Swartz has published the obituary for the mosaic fungus, and I hope he has. It will be well to wait until others corroborate his findings. I am inclined to believe that they will be corroborated.

I have always been in doubt about the so-called mosaic fungus and have had good reason for being in doubt. When Lewis and I read our paper, we thought the evidence at that time was in favor of its being a degenerated pathogen. Unlike Dr. Williams, I have, on several occasions, seen a pathogen run right into a mosaic formation, but of course was never able to cultivate it. We have never seen the mosaic growth in diseases such as pityriasis rosea and psoriasis, but we always find it in keratolysis exfoliativa and frequently in dermatophytosis and dermatophytid. I have never been willing to record a positive finding when only a mosaic formation was found. While the excellent work of Swartz has probably ended a long controversy, there may still be a true mosaic fungus and a pseudomosaic fungus. Time will tell.

DR. FRED D. WEIDMAN, Philadelphia: I gave cotton blue a trial after I found that Dr. Hopkins was using it in his laboratory. In materials from cultures it

is the method of choice for staining fungi. Langeron covered it in his "Précis de microscopie." However, his citation was for material in culture and not in scales. In my own work I had always felt that it was not feasible to employ cotton blue or any other dye in thick samples of material, such as come from between the toes. In these it is necessary also to soften and clear the scales, and potassium hydroxide is incompatible with dyes in general because it destroys their properties. I take it from this method of Dr. Swartz that the hydroxide must be thoroughly neutralized before the lactophenol is used. However, Dr. Swartz' illustrations speak for themselves, and this method should be given a thorough trial.

In the absence of any promise from the preliminary use of potassium hydroxide I turned to glycerin. This is successful for thin scales such as are found in tinea cruris and tinea versicolor and does not interfere with the staining by cotton blue or other dyes. It acts satisfactorily as a clearing agent but is useless if materials are thick.

As to the mosaic fungus, when I first studied dermatophytosis I thought the best position was to maintain that it was truly a fungus, because at that time the results were not clearcut enough to enable me to take a positive stand one way or the other. In that way the problem was laid wide open for attack by others. I had tried the wet Giemsa technic, which stains this type of growth fairly well. I had observed that it dissolved in alcohol, but that was what could be expected from fatty degenerated protein of various origins. In short, I could not secure any direct evidence. After that, it was and still is difficult for me to understand how a nonvital material could so consistently assume the cylindric form that it does between cells. If one thinks of the multitudinous and variously shaped little crevices into which soaps and lipids can go in such places as intercellular clefts, I think it is remarkable that the mosaic fungus should take on so closely the cylindric shape.

As to the absence of intercommunication between mosaic forms and "long" fungus forms, this might be accounted for by the differing times at which the two sets of fungi develop. The residue of fungus which was laid down a month before would not necessarily have any connection with a recurrence of fungus. This recent work of Dr. Davidson and Dr. Swartz is in the right direction, and the burden of proof will now be shifted to those who held that the mosaic formation was truly a fungus.

Dr. Harry R. Foerster, Milwaukee: At the meeting of the American Medical Association in May Dr. Davidson, of Winnipeg, will present a paper on the so-called mosaic fungus, which he will demonstrate to be an accumulation of cholesterol crystals. His article and the accompanying photomicrographs are, to my mind, sufficiently convincing to clarify this controversial subject.

Dr. Karl G. Zwick, Cincinnati: Congratulations to Dr. Swartz are in order for his method of direct examination for fungi in the skin. However, rather than to Dr. Swartz, I extend my felicitations to the dermatologist in practice, to whom simple diagnostic procedures suitable for use in the office are always welcome.

The possibility, mentioned by Dr. Weidman, of replacing the alkaline hydroxide by an acid recalls to my mind the use of formic or glacial acetic acid by French dermatologists, although Darier gave preference to Langeron's preparation of chlorlactophenol. Whereas the alkalis react with the fatty materials present in the skin to form soaps (potassium or sodium stearate, palmitate, oleate, etc.),

which because of their low degree of solubility are difficult to remove by washing, the formation of soaps may be avoided by the use of acids.

It would seem feasible also, if the alkalis and their subsequent complete removal are essential for Dr. Swartz' method, to convert the excessive alkali into salts by means of dilute acid. The cholesterol is removable by ether.

DR. J. H. SWARTZ, Boston: This method takes just two steps longer than that using potassium hydroxide, a total of less than five minutes. We had no difficulty in washing out the potassium hydroxide. We also found strong solutions of potassium hydroxide unnecessary, for the lactophenol continued the work the potassium hydroxide had started.

In answer to Dr. McCarthy's question, I would say that Sabouraud used Sahli's blue and did not use potassium hydroxide or lactophenol. I understand that by this method the preparation of hair was stained successfully but I do not believe that the results were so good with the epithelial squamae.

It is necessary to get the right type of cotton blue. Some commercial houses sell methylene blue as cotton blue. It is necessary to get C4B Poirrier, which may be obtained from the National Aniline Chemical Company, Inc.

If the mosaic formation is not fungus, then what is it? One must admit that it is frequently found in association with normal fungi. Is it not possible then, that the mosaic material is the product of an enzyme action on the epidermal cells set up by the fungi?

We have no difficulty with thick scales and material from the nails if we use an alcoholic solution of cotton blue (1 per cent) and then mount the material in clear lactophenol.

STUDY OF A GROUP OF HANDLERS OF ARSENIC TRI-OXIDE

H. G. IRVINE, M.D.
AND
D. D. TURNACLIFF, M.D.
MINNEAPOLIS

This paper is concerned with recording the findings in a group of patients who were employed in a so-called mixing mill,[1] in which "poison bait" containing arsenic tri-oxide was mixed for distribution to farmers to fight a plague of grasshoppers.

Much has been written on poisoning with various arsenical compounds, and there is little new to be added to the strictly medical knowledge. However, the increasing importance of occupational diseases to medicine in general and of occupational dermatoses to the dermatologist justifies the publication of information on new or different occupational hazards.

A survey of a number of books [2] on toxicology and industrial diseases, several of which were published as late as 1934, failed to disclose any mention of such occupation or any reported cases of poisoning in connection with the mixing of poisoned bait. Neither has any mention of it been found in other literature. This is, no doubt, due to the fact that it has been many years since there has been a grasshopper plague of important proportions.

Owing largely [3] to the extreme and continued lack of moisture in many sections of the farm country of the northwest during 1931, 1932,

---

Read at the Fifty-Eighth Annual Meeting of the American Dermatological Association, Inc., White Sulphur Springs, W. Va., May 3, 1935.

1. This work was undertaken as an emergency after a number of employees were affected and, necessarily, scientific studies had to be secondary to treatment and prophylaxis of the workers. The work was limited to a short season; therefore, the studies were also limited as to time.

2. (*a*) White, R. Prosser: The Dermatergoses or Occupational Affections of the Skin, New York, Paul B. Hoeber, Inc., 1929. (*b*) Legge, Thomas: Industrial Maladies, New York, Oxford University Press, 1934. (*c*) Occupation and Health; Encyclopedia of Hygiene, Pathology and Social Welfare, International Labour Office, Boston, World Peace Foundation, 1930, vol. 1. (*d*) Hamilton, Alice: Industrial Toxicology, New York, Harper & Brothers, 1934. (*e*) Leschke, Erich: Clinical Toxicology, translated by C. P. Stewart and O. Dorrer, Baltimore, William Wood & Company, 1934.

3. All data relative to grasshoppers, infested areas and control were taken from an article by A. G. Ruggles (Three Years Work Against Grasshoppers in Minnesota, J. Econ. Entomol. **27**: [Feb.] 1934) and from a circular by A. G. Ruggles and T. L. Aamodt (Grasshopper Control, Circular 17, Department of Agriculture, University of Minnesota, May 1932).

1933 and 1934, the menace of grasshoppers increased during that period. Areas in Montana, North and South Dakota, Iowa, Nebraska and Minnesota were affected. In Minnesota the invasion reached the peak in 1932, in which year 3,365,265 acres were heavily infested. In that year the state spent $250,000 for control of the plague, and over 11,000 tons of poison bait was purchased and distributed. The menace decreased during 1933 and 1934 owing to success of control measures and in spite of adverse weather conditions.

In Minnesota the grasshoppers were almost entirely of those native species which are commonly present, but in such numbers as to do little harm. The danger arose, then, not on account of an invasion by some unknown pest but entirely because of the favorable weather conditions which contributed to the development of tremendous numbers of those species ordinarily found here.

The most common species of grasshopper found in Minnesota is the two-striped. Other species of importance in certain areas are the clear-winged, the red-legged, the Carolina and the lesser migratory grasshopper. The two-striped grasshopper measures from 1 to 1¼ inches (2.5 to 3 cm.) in length. The dark reddish color is broken by two distinct yellowish stripes running down the back, beginning at the top of the head and running together on the wings.

The life history of these species is the same. There is only one generation per year; they overwinter in the egg stage, and the eggs hatch from May to June. As the hoppers grow they molt, or shed their skin, from time to time, and when fully grown they undergo the final molt and become winged. They take from forty to sixty days from the time of hatching to reach maturity. Mating and egg laying take place from the latter part of July into October or until the first hard frost or freeze. In ordinary seasons the female lays from one to three egg pods, but under favorable conditions, such as existed from 1931 to 1934, the females deposit from eight to ten pods. These pods contain about forty-five eggs each, are about an inch long and three-sixteenths inch in diameter and are covered with a water-proof secretion. Most of the eggs are found in the top 2 inches of soil. Eggs are laid along the edges of fields, roadsides and pastures, and enough grasshoppers may hatch at the sides of a field to destroy the entire crop in the field.

The most efficient control measures depend on the timely use of poisoned bran mash. The bran is mixed with molasses and water and some compound of arsenic. Crude arsenic is the cheapest, with arsenic trioxide next and sodium arsenate and paris green much more expensive.

Formula used in Minnesota:

Coarse wheat bran	100 lbs.
Arsenic	5 lbs.
Molasses	2 gal.
Water	5 gal.

This mixture is sacked and shipped and is usually spread by hand from sacks or, for large areas, from a wagon box. The grasshoppers die in from twenty-four to forty-eight hours, and if the bait is well scattered there is no danger to livestock or birds.

About the middle of April 1934, a station was opened for the mixing of poison bait. This report is concerned with the men employed in this plant. The building used was an old one which had formerly been used for mixing feed. The arsenic tri-oxide came in barrels containing 250 pounds. The heads of the barrels were knocked off, and the powder was

Results of Routine Examination of Men Reporting no Symptoms of Arsenic Poisoning

Patient	Personal Hygiene	Nose Granular	Nose Ulcer	Skin Burn Dermatitis	Days in Arsenic Room	Weeks Worked in Plant	Arsenic in Urine, Parts per Million*	Comment
1	Fair	0	+	+	1	4	4	Was given 8 Gm. sodium thiosulfate orally two days before examination
2	Good	0	+	+	4	6	2.0	Clinically bad; had had 3 Gm. sodium thiosulfate intravenously
3	Poor	0	+	+	0	7	0.9	Clinically bad; later showed sensitization
4	Good	+	0	0	4	4	0.5	
5	Good	+	0	+	0	5	3.0	Sacker
6	Good	+	0	0	0	3	2.0	Sacker
7	Poor	+	0	+	3	4	trace	Had dementia paralytica
8	Fair	0	+	+	2	1.2	0.6	
9	Very good	+	+	0	0	6	0	Sacker
10	Good	+	0	+	5	6	1.2	
11	Good	0	0	0	0	6	trace	Sacker
12	Fair	+	0	+	1	2	0.2	
13	Very good	0	+	0	0	3	9.3	Sacker; large amount of arsenic found, unaccountable unless dust was swallowed, but no systemic symptoms
14	Fair	+	0	0	2	10 days	0	
15	Good	+	0	0	0	1	0	Sacker
16	Very good	0	0	0	3	3	0	
17	Good	0	+	+	0	6	0.2	

* Examination of urine made from a single specimen.

emptied on the wooden floor, whence it was shoveled into the hopper with the bran, to be mixed later with the molasses. The men working in this room were, of course, the ones most exposed to the dust. Those who opened the barrels and the handy men who carried the tops away came next, and some carpenters who tore down and rebuilt the uncleaned bins had considerable exposure. The men who sacked the mixture handled it only after the molasses had been added and thus were the least exposed.

The men in the mixing room [4] worked eight hour shifts but were supposed to work only one shift a week in this room. On coming to the plant in the morning they took off all clothes but their underwear and

4. Directions of Minnesota Industrial Commission.

put on sox, shoes and jumpers which were kept at the plant. At the end of their shift they were supposed to take showers before changing back to their other clothes. They wore gloves and rubber respirator masks while in the arsenic mixing room. They were not required to wash before eating lunch during their shift, and candy vending machines were present, so that it was possible for the men to buy and eat candy in the plant during their hours of work.

The plant had been in operation under these conditions for about six weeks before May 28, when we were first called on to examine some of the men. The cases described, then, are those of the men who had been working previous to that date and who came to us from time to time during the next few weeks. The cases listed in the table, on the other hand, are those of the men on one shift who were given routine examinations for arsenic in the urine and who, for the most part, showed no cutaneous or subjective symptoms and so were still working.

REPORT OF CASES

CASE 1.—D. B., aged 28, worked in the mixing room shoveling arsenic into the hopper for six days. He was seen three weeks after the contact. There had been a generalized dermatitis, including swollen, inflamed eyelids. The skin cleared after he was in bed for a week. The results of examination were negative so far as the skin was concerned, except for subungual separation. The mucous membrane of the nose was red and granular, and a garlic-like odor could be detected. During the period of illness he lost 12 pounds (5.4 Kg.). Examination of the blood showed a hemoglobin content of 110 per cent, with 6,600,000 red cells and 14,000 white cells.

He was given five doses of sodium thiosulfate on successive days, after which the blood was again examined and showed a hemoglobin content of 80 per cent, 4,000,000 red cells and 9,000 white cells. After an interval of two weeks the blood was again examined, and the hemoglobin content was 101 per cent, the red cells 6,000,000 and the white cells 9,000, as before. He was then given ten additional doses of sodium thiosulfate, and the blood was again examined. The hemoglobin value was 84 per cent, the red cells 4,350,000 and the white cells 6,900. There had been evidence of diminishing vision. After treatment the patient reported that he felt much better. Roentgenograms of the chest were negative.

CASE 2.—J. C., aged 54, worked as a carpenter in the plant, handling lumber that had been in contact with the arsenic and on which there was still dust. He had a generalized dermatitis of the sensitization type, edema of the eyelids and edema of the auditory canal to such an extent that it was closed. The mucous membrane of the nose was red and granular, and there was a good deal of swelling over the septum but no perforation. The urine contained no albumin.

He was given ten doses of sodium thiosulfate and symptomatic local treatment, with good results. One month after treatment examination showed the blood picture to be normal. Contrary to instruction, he returned to the plant after treatment, and he had an immediate recurrence of the same sensitization type. This man's urine showed no arsenic after ten treatments with sodium thiosulfate.

CASE 3.—M. N., aged 47, worked five weeks at the plant, during which time he carried away to be burned the heads which were knocked off the arsenic drums.

He had ulcerating lesions in the groins, scrotum and perianal region as a result of arsenic burns and a blotchy erythematous eruption over the body and on the neck under the collar-band. He had gingivitis and an ulcer on the nasal septum, the tonsils were covered with a necrotic membrane, the glands of the neck were swollen and there was a trace of albumin in the urine.

He improved rapidly after three doses of sodium thiosulfate were given in two days. Two weeks later he returned to the plant. After one day a sensitization dermatitis developed, for which he was given five additional doses of the sodium thiosulfate, with good results. He was not employed again at the plant.

CASE 4.—F. H., aged 31, worked two eight hour shifts in the arsenic room during ten days. He reported for examination two weeks after he was off duty. There had been dermatitis under his mask about the nose and mouth, in the groins and on the back of the neck. On examination, the skin showed no lesions, but there was an ulcer on the septum, and the odor of arsenic was noted on the breath. He was given two doses of sodium thiosulfate and advised against further work at the plant.

CASE 5.—G. F., aged 35, was employed as a sacker for four weeks before examination. He had dermatitis under the wrist band of his sleeves and some small secondary furuncles. The condition cleared following two doses of sodium thiosulfate, and he was able to continue his work under special care.

CASE 6.—E. M., aged 28, was employed as a sacker. It was found that he was working in different shifts in two mills. He had no trouble until an accidental puncture by a needle became inflamed from the contact with arsenic. It cleared after local treatment with packs of sodium thiosulfate solution.

CASE 7.—R. S., aged 52, was employed as a sacker. This man also showed a reaction around a puncture by a needle, with the skin otherwise normal. This cleared with the local application of sodium thiosulfate packs, and he continued employment.

CASE 8.—T. J., aged 45, was employed as a foreman and, as such, was in contact with the different kinds of work for brief periods only. He showed a reddened inflamed cuticle around four finger-nails, with the skin otherwise normal. The condition cleared with local treatment.

CASE 9.—J. S., aged 38, had a contact dermatitis on the face, conjunctivitis of the right eye and an ulcer on the septum. The condition cleared after one dose of sodium thiosulfate, the application of boric acid solution in the eye and rest from work for three days.

CASE 10.—H. A. K., aged 54, was employed as a handy man for four weeks. His job took him into all parts of the plant and exposed him to the dust and other contacts with arsenic. He had an erythematous and papular eruption on the face, chin, neck and groins. There was gingivitis, and the nasal mucous membrane was reddened and rather granular. The urine contained no albumin. There was some odor to the breath. The condition cleared after six injections of sodium thiosulfate, and he was not permitted to return to work. There was no arsenic in his urine after treatment.

CASE 11.—W. H. F., aged 34, worked in the plant three weeks, during which time he served four shifts in the arsenic room. The first indication of trouble came after he had had four days of routine treatment at the plant, consisting of daily oral administration and two intravenous injections of sodium thiosulfate. There was an acute gastro-intestinal upset with vomiting, diarrhea, a temperature of 100 F. and a trace of albumin in the urine. Examination showed a small ulcer on the septum.

The condition cleared after three more intravenous injections of sodium thiosulfate. One could not be sure that the gastro-intestinal symptoms were due to the arsenic. On his return to the arsenic room one month after the disappearance of these symptoms, he had, after one day, an acute dermatitis of the face and arms. This cleared after three injections of sodium thiosulfate intravenously, and he was not permitted to work again except as an outside trucker.

CASE 12.—G. H., aged 22, had worked for four weeks as a sacker. When examined he was found to have a burn with ulceration about one-fourth inch in diameter in the left groin. This was treated locally with sodium thiosulfate solution, and he was permitted to continue work.

CASE 13.—F. W. J. was employed as a trucker but had worked two days in the arsenic room. He had inflamed cuticle around three finger-nails. This cleared under local treatment with sodium thiosulfate solution, and he continued work as a trucker.

CASE 14.—O. H., aged 27, was employed in the arsenic room. He had only a conjunctivitis from dust, and the skin was normal. The condition cleared in three days while he was not working. He was able to continue.

CASE 15.—M. E., aged 26, was employed seven weeks before he reported a dermatitis around an abrasion of the skin on one finger and a slight folliculitis on one arm. On examination, it was found that he had a perforated septum, of which he was entirely unconscious. There was no evidence of any infection, and the Wassermann reaction was negative, so it might be assumed that the nasal condition was due to arsenic. If so, it would agree with the findings of others that perforations may occur without subjective symptoms. The skin cleared with local treatment.

CASE 16.—A. O., aged 34, was employed as foreman. This case is interesting since he appeared with reddened inflamed cuticle around each finger-nail several weeks after the routine care with oral and intravenous administration of sodium thiosulfate had been established. Two weeks after this he had a generalized urticaria associated with alcoholic intoxication, and there was a slight dermatitis following the urticaria. Whether the scratching or the arsenic was responsible for the dermatitis is a question. The blood picture at this time was normal. He was given three doses of sodium thiosulfate and was not permitted to return to work.

CASE 17.—J. A. F., aged 29, was employed as foreman. A sensitization dermatitis developed while he was under the routine treatment, which included thirteen intravenous injections of sodium thiosulfate. He was then away for three weeks, after which he returned for one day to help clean up after the plant was closed and immediately suffered a recurrence.

CASE 18.—F. F., aged 67, father of J. A. F. (case 17), was employed as handy man and carpenter. He had a history of an acute cutaneous reaction in May, with ulcers on the septum. This cleared while he was at work and receiving the routine treatment at the plant, which included thirteen intravenous injections of sodium thiosulfate. Later, he returned with his son to the plant to help clean up the building, and he too suffered a recurrence.

CASE 19.—J. D., aged 39, went to work on May 6 and for two days worked outside trucking. On May 8 he went to work in the arsenic room and worked on eight hour shifts from then until he was laid off on May 17. He began to have trouble with his skin at the end of the first day, and this increased until he stopped work. There were reddening of the face, swelling of the lids, irritation of the

skin of the genitals and wrists and soreness of the nose and throat with hoarseness. After he stopped work all the symptoms involving the skin and mucous membrane subsided except the lesions on the scrotum. He lost a few pounds in weight. When he was seen on July 20, nine weeks after exposure, his urine showed 0.15 parts of arsenic per million. After one dose of sodium thiosulfate, the urine on August 1 showed 0.07 parts per million, and on August 7, after he had had five more treatments with sodium thiosulfate, the urine showed no arsenic. This was the only case in which we had the opportunity to make repeated tests of the urine.

COMMENT

A study of the case records confirms the findings of others [5] as to the susceptibility of certain areas of the skin, such as the cuticle around the nails, the groins and scrotum, the neck and areas where the clothing may rub the dust into the skin. We have also found the mucous membrane of the nose to be consistently affected. Breaks in the skin [6] were a source of trouble when the rest of the skin might be normal.

In general, we have observed the cases in which only the mucous membrane was affected, the cases in which the dust had a purely local effect, acting as an escharotic, and the cases in which there was a generalized dermatitis of the sensitization type. With the local reactions there is a possibility that, under treatment and with proper care, a man may continue his work, but with the sensitization type, while the response to treatment is satisfactory, there seems to be no possibility that the man can stand the slightest exposure without expecting a recurrence.

In taking over the care of the men who were working, we arranged to have jumpers changed daily instead of weekly. The exposed skin was greased, and an oil was used in the nose at least twice daily. Each man took a shower at the end of his shift and washed exposed parts and groins with a solution of sodium thiosulfate. No food was allowed in the mill on account of the danger of ingestion of the arsenic, and no food was allowed to be eaten during the time a man was on the shift. In addition, of course, in a proper building much could have been expected from the right ventilation.

Because this was a short, seasonal and almost an emergency job, we gave each worker the choice of taking either 1 Gm. of sodium thiosulfate orally twice daily or at least two doses per week intravenously. As a matter of fact, practically all of them took both.

There is a considerable literature on laboratory findings in connection with arsenic poisoning. Except for the general observation that arsenic seems to find its way into certain tissues, the findings are not always in accord. This is especially true in relation to what happens when an

5. Legge,[2b] p. 79.

6. White,[2a] p. 169.

arsenic-affected patient is given sodium thiosulfate. Some authors [7] have stated definitely that there is an increase in the arsenic content of the urine when the sodium thiosulfate is given, and they argued that this accounts for the clinical improvement of the patient. Others [8] stated that there is a decrease in the amount of arsenic in the urine after the administration of sodium thiosulfate, and that this drug simply fixes the arsenic in the tissues in a nontoxic state. One author [7] went so far as to claim that there was a marked increase in the amount of arsenic in the hair after the administration of sodium thiosulfate, although, if we are to believe our own teaching that the visible hair is dead, we do not see how it could get there, especially until such time as a considerable amount of new hair was available.

The one case in which we had opportunity for repeated tests of the urine showed decreasing amounts of arsenic after the administration of sodium thiosulfate. In three other severe cases there was no arsenic in the urine after a number of intravenous injections of sodium thiosulfate.

It seems strange and a matter of considerable importance that, in spite of the fact that sodium thiosulfate has been used by dermatologists for years with great satisfaction, no book on toxicology or industrial medicine to which we referred, even up to 1934 editions, includes mention of this remedy for arsenic poisoning.

One patient studied (case 1) showed the stimulating effect of the arsenic on the hematopoietic system and also the effects of the sodium thiosulfate on the findings from hematologic examination.

Study [9] of the literature indicated that arsenic is found in the urine in variable amounts in as high as 40 to 50 per cent of supposedly normal persons. Our table of urinary findings in a group, most of whom had not been reported to us for clinical symptoms, seems to indicate that even large amounts can be present without giving rise to cutaneous or subjective symptoms.

Considering these two points, one wonders whether it is entirely fair to assume that any dermatosis is due to arsenic simply because of the finding of arsenic in the urine, especially since it is quite possible to find some arsenical contact for almost any patient if one starts out to do so.

---

7. Althausen, T. L., and Gunther, L. M.: Acute Arsenic Poisoning, J. A. M. A. **92**:2002 (June 15) 1929; quoted by Ayres, Samuel, Jr., and Anderson, N. L.: Cutaneous Manifestations of Arsenic Poisoning, Arch. Dermat. & Syph. **30**:33 (July) 1934. Meyers, C. N., and Groebel, M. R.: Therapeutic Activity of Sodium Thiosulphate, Proc. Soc. Exper. Biol. & Med. **23**:97, 1925.

8. Use of Colloidal Sulphur in Arsenical Dermatitis, Queries and Minor Notes, J. A. M. A. **99**:1374 (Oct. 15) 1932. Ullmann, K.: Dermat. Wchnschr. **82**:11 (Jan. 2) 1926; quoted by Pusey, W. A., and Senear, F. E., in Year Book of Dermatology, Chicago, Year Book Publishers, 1926, p. 197.

9. Halloran, Chris: Dermatitis Exfoliativa Due to Arsenic in Wall Paper, Arch. Dermat. & Syph. **20**:303 (Sept.) 1929.

SUMMARY

A description of the problem of the grasshopper plague and the means used to combat it is given.

Presentation is made of a group of cases of workers in a mixing mill who were affected by the arsenic in the poisoned bran.

A table of urinary findings in a group of workers showing almost no clinical symptoms is given.

Comments are made on methods for the care of workers, laboratory findings and the conclusions drawn from these findings.

ABSTRACT OF DISCUSSION

DR. SAMUEL AYRES JR., Los Angeles: I was much interested in Dr. Irvine's remarks about the finding of arsenic following the administration of sodium thiosulfate. Although no arsenic was found after ten injections, this does not eliminate the fact that sodium thiosulfate does increase the output of arsenic. My associates and I have made it a rule to examine a twenty-four hour specimen of urine by the Gutzeit method prior to giving any injections. We then give 1 Gm. of sodium thiosulfate intravenously and collect about a quart (960 cc.) of urine immediately following the injection. We have found a considerable increase in the output of arsenic following the injection, in many instances as much as ten times the previous output. We have used only the soluble form of sodium thiosulfate. After the preliminary increase of output, the continued administration of sodium thiosulfate every second or third day finally results in a progressive decrease, and within one, two or three months, depending on the amount of arsenic present, the urine becomes absolutely free. I think this finding is significant, especially in view of some recent statements to the effect that sodium thiosulfate is of no value in the treatment of arsenic poisoning. In his book on syphilis Moore made the statement that it is of no benefit, but I think we should not say this in view of the fact that the output of arsenic is immediately increased after injection and that there is later a diminished output as clinical improvement occurs.

DR. KARL G. ZWICK, Cincinnati: Since arsenic can be found by spectrographic methods almost everywhere, it has become necessary to make quantitative determinations in order to establish whether its presence is dangerous.

The problem touched by Dr. Irvine is of interest not only to the agriculturist but also to the consumer who ingests the farm products to which arsenical compounds have been applied more or less generously. Protracted consumption of farm products contaminated with arsenic may, in the course of time, produce toxic symptoms through cumulation or through sensitization. However, it would also seem at least theoretically possible that "arsenic-fastness," an increased tolerance for or increased resistance to arsenic, may gradually develop.

DR. EARL D. OSBORNE, Buffalo: I wish to call attention to one phase of the subject which may be of practical benefit to those who practice dermatology where there are large orchards and vegetable farms. My associates and I have treated a number of patients with severe dermatitis venenata which we have demonstrated to be due to the arsenic in spray residues on the fruit and vegetables. Fruit and vegetable handlers are definitely liable to a contact dermatitis due to exposure to sprays containing arsenic.

DR. GEORGE MILLER MACKEE, New York: There has been a great deal of work done biochemically on the dermatoses due to arsenic, with considerable agreement among different persons in finding arsenic in the skin. Dr. Gaul, a member of my staff, has been doing a good deal of work spectroscopically, and a problem has arisen. The work has not proceeded very far, but he has failed up to this time to find arsenic in excess in the skin for more than a few hours after the administration of one of the arsphenamines. His findings thus far do not corroborate the chemical findings. There must be an error somewhere, on the part of either the physicist or the chemist. We have wondered whether the dermatoses might not be due to sensitization rather than to retention of arsenic in the skin.

DR. A. BENSON CANNON, New York: I should like to express my pleasure in having heard Dr. Irvine's excellent paper. I think such observations as he has made on acute arsenic poisoning will aid in interpreting the findings of arsenic retention in patients having obscure dermatologic conditions as well as in those suffering from acute arsenic poisoning. My associates and I are seeing an increasing number of patients who have gone from one clinic or from one physician to another over a period of years, the diagnosis varying with each physician or clinic consulted. In these cases, we have found large quantities of arsenic in the blood, urine and skin, and on giving sodium or calcium thiosulfate, we have noted an increased excretion of arsenic in the urine, and there has usually been a clearing of the lesions of the skin. I feel reasonably certain from our investigation that many of the cases of so-called ptomaine poisoning in which there are acute gastrointestinal upsets with abdominal cramps, diarrhea, nausea, vomiting, soreness of the mucous membranes of the mouth and throat, sometimes ulceration of the oral mucous membranes and conjunctivitis are cases of acute arsenic poisoning. When one of these patients has fever and generalized erythema of a scarlatina type, a diagnosis of scarlet fever is frequently made. I think that in many cases of aplastic anemia in which there is retention of arsenic the anemia can be definitely attributed to arsenic poisoning. Agranulocytic angina has been reported as following the administration of arsphenamine.

Much evidence is accumulating showing that acrodynia and Raynaud's disease as well as other vascular disturbances of the extremities are perhaps due to arsenic.

The sources of arsenic intake are so numerous and variable that few persons, if any, escape some retention. While acute arsenical poisoning as observed by Dr. Irvine is, within itself, most important, I think that if he is able to follow the same patients over a period of years he will be able to present even more valuable data on the effects of chronic retention of arsenic.

DR. H. G. IRVINE, Minneapolis: I appreciate the discussion and wish to emphasize again that this was an emergency task and that there was no opportunity to study cases except during a limited period because of legal involvement. I regret that we did not have the opportunity to carry out the study we should like to have made. We could offer only what we had. A single sample of urine was obtained, and we had to take that when we could get it. There were no twenty-four hour specimens. The men were eager to retain their jobs. There was one case in which we had an opportunity to examine the urine three times within a short period, and in that case there was a decrease of the output of arsenic. I think a study of these patients over a long period would be valuable. This sort of study has not been made by men qualified to do the work, so far as I could find in the literature.

LICHEN SIMPLEX CHRONICUS

ONE HUNDRED AND SEVENTY CONSECUTIVE CASES ENCOUNTERED IN PRIVATE PRACTICE

D. E. H. CLEVELAND, M.D., C.M.
VANCOUVER, CANADA

The generally accepted view of lichen simplex chronicus is that it is a cutaneous reaction which may be evoked by a number of different agencies acting on the skin of predisposed persons. Its clinical characteristics are well defined: A patch of closely aggregated papules and pseudopapules develops on certain areas of predilection, exhibiting as secondary changes chronic leathery thickening, pigmentation and usually exfoliation of minute scales, accompanied invariably by intense pruritus which is characteristically paroxysmal.

Emotional and nervous disturbance has generally been considered to be an important, if not the chief, factor in the etiology. This opinion is reflected in the common designation by such terms as neurodermitis, the English rendering of the name given it by Brocq—*névrodermite*—and neurodermatitis. In a recent paper Pels [1] drew a clear distinction between the proper use of the terms neurodermitis and neurodermatitis. When writing my previous paper on this subject [2] the distinction was not clear to me, but in this paper the identity of Brocq's neurodermitis with Vidal's lichen simplex chronicus is accepted. It is commonly held that the pruritus is antecedent to the objective cutaneous changes and that the latter are largely the result of friction and trauma—frequent and vigorous rubbing and scratching—to the pruritic area. An increasing number of observers have expressed the opinion that the pruritus is an expression of allergy.[3]

Whether allergy is to blame or not, the neurogenic aspect may not be disregarded entirely. Are patients with this disease "neurotic," that is, persons whose threshold for neurogenic and psychogenic stimuli is unusually low? Or are they subject by their environment to unusual nervous and emotional strain? In a number of cases the patient appears to belong to one or both of these categories, as pointed out by Stokes.[4]

Read before the Section on Dermatology and Syphilology at the Eighty-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1935.

1. Pels, I. R.: The Neurodermatoses, Internat. Clin. **4**:280 (Dec.) 1934.
2. Cleveland, D. E. H.: Lichen Simplex Chronicus, Canad. M. A. J. **29**:368 (Oct.) 1933.
3. Wise, F., and Ramirez, M. A.: Protein Sensitization in Pruritus with Lichenification, Arch. Dermat. & Syph. **11**:751 (June) 1925.
4. Stokes, J. H.: The Effect on the Skin of Emotional and Nervous States, Arch. Dermat. & Syph. **22**:803 (Nov.) 1930.

Among other etiologic factors, local physical trauma, reflex vasomotor disturbances, age, sex and the coexistence of other cutaneous or visceral disease are commonly cited.

In the endeavor to utilize data obtained from personal experience in considering these questions I have studied 170 consecutive cases taken from 5,000 cases of diseases of the skin observed in private practice. This represents an incidence of 3.4 per cent in private practice. Before collating these figures there was an impression that the incidence was much higher. Figures showing the relative merits of roentgen versus medicinal therapy for this disorder are also presented.

ANALYSIS OF CASES

The series has been analyzed under the following headings: age and sex, complexion, duration, history of preeruptive pruritus or injury, history of allergy, coexisting disease, habits, occupation, location and treatment.

Age and Sex.—The incidence according to age showed a rapidly mounting curve from 5 cases in the first decade to 40 in the fourth, with a more gradual decline to 4 cases in the eighth. Fifty-seven per cent of the patients were between the ages of 31 and 50. There were contrasting curves for the sexes according to age. Fifty-six per cent of the cases in men occurred in the fourth and fifth decades, while only 33 per cent of the cases in women occurred in these decades. The decade in which the greatest number of cases (20) occurred in women was the third, but with this exception the curve was fairly level from the second to the seventh decade, the variation being between the extremes of 10 and 14 cases. The average incidence according to age in females was 38.35 years, and in males, 39.30. While it is a disease of early middle life, the figures show that it occurs in men chiefly in middle age, whereas women are liable to it at any time between the period of adolescence and old age. It has not been observed to be associated especially with the climacteric.

Ninety-four cases were in females and 76 in males.

Complexion.—A marked difference was shown between the incidence in blonds (including 1 rufous blond) of 48 cases and the incidence in brunettes of 122 cases. Figures are not available concerning incidence according to race in general, but the proportion occurring in Orientals (Chinese and Japanese) seemed significant, if only to emphasize the predilection of the disease for a dark skin. Brandt,[5] in noting an

5. Brandt, R.: Die Abgrenzung der Neurodermitis vom chronischen Ekzem auf Grund konstitutioneller Betrachtung, Dermat. Ztschr. **65**:330, 1933.

extensive list of constitutional characteristics which occur in cases of neurodermitis which distinguish it from chronic eczema, mentioned its prevalence in persons with dark hair and dark eyes. Although only 2.75 per cent of the total of 5,000 cases of diseases of the skin occurred in Orientals, 6.52 per cent of all the cases of lichen simplex occurred in Orientals. This would suggest that the disease occurs more than twice as frequently in Orientals as it does in members of the white race.

Duration.—Chronicity was well exhibited, the duration in several cases being more than ten years, and the average duration when the patients were first seen by me being five years. Most of the patients over a year old had already had medical attention, and the condition had been diagnosed as eczema.

History of Preeruptive Pruritus or Injury.—It was considered significant that in 80 cases there was a clear and decided history of local itching preceding the appearance of the lichenification. In a relatively small number of cases in which there was a history of antecedent pruritus there had been some other cutaneous involvement, but this did not always include the area on which the lichenification had developed. In many of these cases the antecedent cutaneous disease had persisted and was visible on other parts of the body unaffected by lichenification. In 16 cases the pruritus with subsequent lichenification had developed on the site of an injury to the skin which had occurred several years previously. In none of these cases were the scars hypertrophic, contractile or otherwise conspicuous or abnormal.

History of Allergy.—In 30 cases there was a history of allergic phenomena: asthma, hay fever, repeated attacks of urticaria and eczema. In 4 cases there was no personal history of allergy, but relatives had suffered from such a condition. In 8 cases there were both a personal and a family history of allergy. Brandt [5] stated that a positive cutaneous reaction to tests with allergens is uncommon but expressed the opinion that a latent allergic state is often an etiologic factor.

Coexisting Disease.—In 49 cases another cutaneous disease was present, in the majority of which there appeared to be a definite relationship between the cutaneous conditions, the lichenification appearing in close proximity to areas otherwise involved. In 19 cases there was diagnosis of seborrheic dermatitis, in 3 of psoriasis and in 10 of eczema.

The remaining coexisting dermatoses included such conditions as radiodermatitis, scabies, dermatitis venenata and industrial dermatitis. In practically all the cases the lichenification was discovered in the course of examination and was not the complaint for which the patient presented himself, appeared to have no relation to and probably antedated the other dermatosis. In 1 case typical acute generalized lichen planus

with no history of previous attacks occurred in a patient who had lichen simplex chronicus of the nucha of many years' duration.

There were 29 cases in which noncutaneous disease was present. These included 12 cases of metabolic or endocrine dysfunction: 4 of diabetes, 4 of hyperpiesis, 2 of organic disease of the central nervous system and 1 each of epilepsy and Korsakoff's syndrome (alcoholic polyneuritis and disorientation).

In addition, there were 34 cases in which an organic disease was not known to be present but in which the patient was noticeably of the type colloquially referred to as "neurotic," "hysterical" or "mental."

The small number of cases (38) in which organic or functional nervous disturbance occurred is regarded as a reflection on the validity of the names neurodermitis and neurodermatitis applied to the disease. Such names imply that the neurologic factor is predominant in all cases. It was notable that self-possessed, apparently well balanced, often rather stolid persons were in the majority in this series. Many, it is true, complained of loss of sleep and similar annoyances from itching, but few appeared to suffer from any resulting nervous disturbance. The latter were mostly included among the 34 "neurotic" patients. One of them, a Jewish executive in a position involving much responsibility, had suffered severely from lichen simplex chronicus of the perineum, lost much weight as well as sleep and was seriously contemplating suicide. He responded well to treatment and was seen six years later in good health. During the seventh year he consulted me for severe pain following zoster and hyperesthesia in the costal region, which yielded promptly to treatment.

Three patients are known to have died, 1 of carcinoma of the intestines and 2, suddenly, of cardiac disease. One of these had been treated successfully by me for alopecia areata three years prior to the development of lichen simplex chronicus.

One patient, who at the time he was treated for lichen simplex chronicus could not furnish a history suggestive of allergic reactions, consulted me again five years later when suffering from distressing generalized urticaria which followed a severe nervous shock.

Many of the women reported premenstrual exacerbations. They had no history of gynecological disturbance and presented no symptoms which justified calling a gynecologist in consultation. On these grounds I consider that they probably did not suffer from a pelvic disorder. A few patients volunteered the observation that they had more inconvenience when they were constipated. Intolerance for fur and wool was rather a frequent complaint.

Four patients attributed the disease to local dampness connected with their occupation. One said that irritation was caused by the pressure of kneeling on damp wool, a wet spot coming in the clothing covering

his knee when he was playing the game of curling on the ice. There was a remission each summer, with recurrence when he resumed his favorite winter pastime. Two others stated that their work involved continuous dampness about the legs and feet, that at work they constantly wore high boots and woolen clothing below the knee and that intense itching always followed the removal of clothing at night, which was noted long before the thickening of the skin became apparent.

A few patients, while not giving a history of typical allergic reactions, named certain articles of diet which they believed aggravated or precipitated attacks of itching; among the foods more frequently mentioned were tomatoes, berries, cheese and bacon. None blamed alcohol or tobacco. One said that the itching was less troublesome when he was drinking more than usual.

Only 1 patient blamed his occupation directly. He was employed on a barge and his clothing was constantly impregnated with cement dust and coal dust; there were several patches of the disease on the inner surface of the lower portion of the thighs and on the legs.

These data indicate that one or more itching spots may occur on the skin, initiated by a variety of causes. Among these causes, allergy is important, and it is believed that just as the urticarial wheal, the erythematovesicular plaque of eczema and congestion of the mucosa of the upper or lower respiratory tract are primary expressions of the allergic reaction, so in many instances is the localized pruritus which precedes visible alterations in the skin. That there is a constant relationship between lichen simplex chronicus and other diseases, either cutaneous or visceral, does not appear justified. That a lowered threshold to nervous or psychic stimuli is a contributory factor in a small proportion of cases appears to be true, but this does not justify calling the disease a cutaneous neurosis.

Habits.—A history of dietary indiscretions of a character generally considered to be conducive to aggravation or precipitation of pruritus (the popular term "heating to the blood," although inaccurate, is graphically descriptive) was obtained in only a small proportion of cases. In 11 there were gross errors of diet, with an excessive proportion of protein or carbohydrates, overeating or hasty eating. In 8 there was excessive smoking. Six patients indulged to excess in alcoholic beverages and 7 in tea or coffee, and 2 were addicted to the excessive use of condiments.

It is believed that dietetic faults, while contributory, are not a primary etiologic factor.

Occupation.—Examination of the figures relating to the occupations of the patients does not furnish any information of significance. Fifty-eight patients were housewives, being married or single women living

at home, with no regular outside occupation. Ten were stenographers. The remaining 102 patients were engaged in forty-six different occupations, trades and professions. One would not gather that any importance attaches to occupations as an etiologic factor. A much larger series of cases might furnish more significant figures, especially with a larger proportion among members of the professions and workers in various fields of imaginative art if the neurologic aspects of the disease are to be supported.

Location.—The number of cases in which several areas were involved and the number in which either a single area or two symmetrically disposed areas were affected were about equally divided. Of the latter there were 83 cases, and the disease was exhibited in eighteen

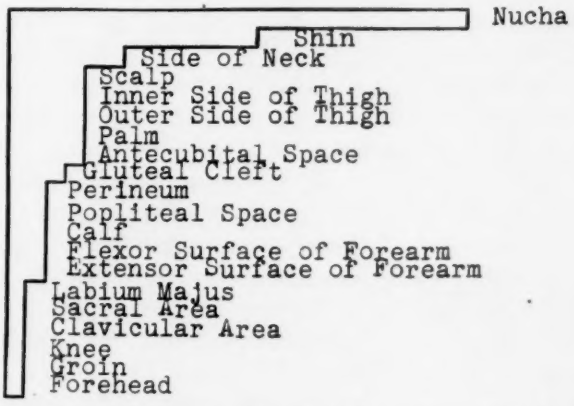

Fig. 1.—Sites of predilection in cases of single or symmetrical involvement.

different areas. In the 87 in which there was multiple localization, thirty-three areas were involved 253 times.

The nucha was a site of predilection par excellence. In the 83 cases in which there was a single or two symmetrical areas the nucha was the site 24 times. In the 87 cases of multiple localization the nucha was involved 43 times. Almost without exception these cases occurred in women. There are several reasons. Some of the patients with the worst condition wore their hair long and done up in a large knot at the back. These women are more likely to neglect the care of the scalp than women who cut their hair, and seborrheic dermatitis is more prevalent. Local warmth, moisture and lack of ventilation at the margin of the occipital portion of the hairy scalp under the heavy knot and the frequent small injuries from hairpins and the teeth of combs, which are always used here with an upward stroke directed against the lower occipital protuberance, combine to produce a constant condition of mild irritation. The inevitable habit of scratching is often performed unconsciously and

sets up the vicious circle of which lichenification is one of the portions and the objective evidence.

Corson,[6] in his observations on naevus flammeus nuchae, stated that the usual outbreak in that abnormality is of the nature of a seborrheic or eczematoid dermatitis, with occasional resemblance to psoriasis. This nevus has been observed frequently in the absence of lichen simplex chronicus, and when it has been observed coexisting with the latter disease there have been only small patches of lichenification.

The sides of the neck and the antecubital and popliteal areas are the next most frequently affected parts. These regions not only fre-

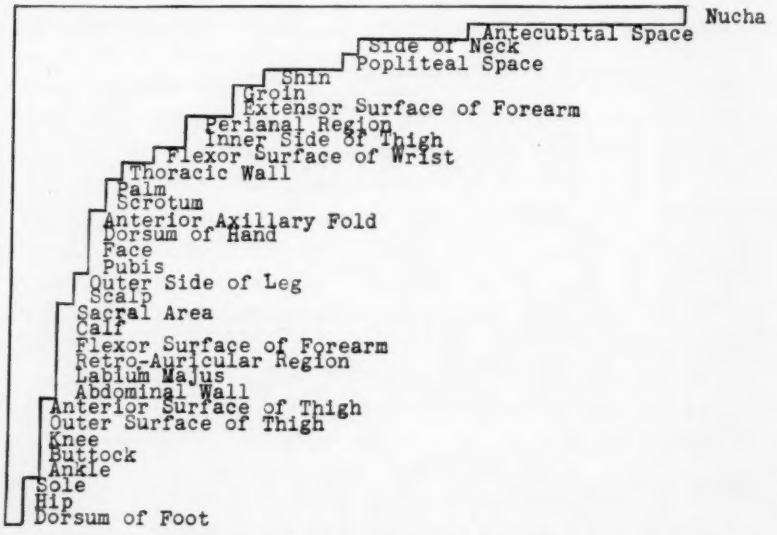

Fig. 2.—Sites of predilection in cases of multiple involvement.

quently exhibit dermatitis from various causes but when, as is usual, they share in a more general inflammatory condition they are slow to recover. A natural corollary is that these areas are scratched and rubbed for a much longer time than the other parts.

Friction, chafing, irritation from decomposing sebum, sweat and epithelial débris are accountable for the frequency of lichenification in the groin, the genitocrural regions and the gluteal cleft. Three men with the condition in the gluteal cleft wore heavy woolens, and the lichenized areas had clearly developed in connection with intertrigo. On the shins it was repeatedly observed that pruritus was initiated by wearing woolen socks. When the socks were removed at night the skin itched, and the patient devoted a few moments to scratching. This had

6. Corson, E. F.: Naevus Flammeus Nuchae, Am. J. M. Sc. **187**:121 (Jan.) 1934.

developed into a bedtime habit long before a visible change occurred in the skin. A change of the type of clothing, together with avoidance of other forms of irritation, such as heat and soapy bathwater, was sufficient in early cases of this type to effect a cure.

Bony and muscular prominences exposed to frequently repeated small traumas are evidently the areas of predilection for lichen simplex chronicus. Small injuries are most frequently of the nature of friction and pressure. Other sources of irritation, such as reflex itching and neurovascular disturbances, whether of allergic origin or not, cause phenomena on other areas it is true, but rarely do they cause constant scratching and rubbing confined to a relatively small circumscribed area except over the prominences. The element of trauma is an inseparable part of the picture.

Treatment.—As itching is a constant component of the vicious circle with which one has to deal, it appears axiomatic that unless itching is checked cure is impossible. To reduce the infiltration at the same time the pruritus is controlled, the most readily applied and rapidly successful means in the experience of most workers has been the roentgen rays.

In my series a number of patients were for various reasons treated by other methods than roentgen rays, but there was no attempt to make exact comparisons by such a method as giving treatment in alternate cases by roentgenologic and other methods. Those patients not receiving roentgen therapy received antipruritic and keratolytic remedies in the form of lotions, ointments and pastes. The definition of the terms used—cured, relieved, improved, not improved and not treated—is for the sake of convenience somewhat arbitrary.

The patients cured, of whom there were 15, had no itching or objective signs one year after treatment. Of these, 14 were treated with roentgen rays, the dose being from ½ to 2¼ skin doses, with an average dose of 1.07 skin doses.

Twenty-seven patients were relieved with cessation of itching and partial or complete disappearance of the objective signs when treatment was discontinued, but the subsequent condition was unknown. Of these, twenty-six were treated with roentgen rays, the dose being from ½ to 4 skin doses, with an average dose of 1.2 skin doses.

In 73 patients the condition was improved. Treatment was discontinued owing to failure to improve by the time a safe limit of dosage had been reached, without complete relief from itching, or for other reasons unrelated to the disease or to the treatment. Of this group, 58 were treated with roentgen rays.

In 20 the condition was not improved. Treatment was discontinued by the patient before satisfactory results were obtained, in most cases probably because of dissatisfaction. Thirteen were treated with roentgen rays.

The remainder of the patients were not treated. Only a diagnosis was made, although a certain number of the patients were given some topical medication, and from them nothing further was heard. In 2 of the cases diagnosis was made on the basis of the history only, since the patients had been overtreated by a radiologist, with resulting radiodermatitis and depilation of the occipital portion of the scalp.

No other treatment was given in association with the roentgen therapy except a mild antipruritic lotion, such as hamamelis or phenol, and an occasional compound of barbituric acid. The dosage never exceeded one-fourth skin dose weekly, and in those cases in which a total of 2 skin test doses was exceeded, an interval of at least six months elapsed before treatment was resumed beyond this dosage. No untoward effects of the roentgen rays were observed or reported.

Advice concerning dietary restrictions was given; suspected or detected allergic or other irritants were removed from the diet and the environment; habits were regulated; a hygienic regimen was instituted, and whenever possible treatment of other suspected sources of difficulty, such as infective foci and metabolic disturbances, was arranged.

The roentgen rays furnish the most convenient and rapidly successful method of treatment, and the average dose necessary is between 1 and 1½ skin dose.

SUMMARY

Lichen simplex chronicus occurs principally during adult life, usually appearing later in men than in women and considerably more frequently in women.

The disease occurs almost three times as often in brunettes as in blonds and more frequently in Japanese and Chinese than in people of European origin.

While preserving a strict identity, it often occurs in association with other chronic diseases of the skin and is commonly confused with them by the physician.

The neurogenic factor does not occur with sufficient frequency to justify regarding the disease as a cutaneous neurosis or giving it a name implying a constant neurogenic etiology. Consideration of the proportion of cases occurring in various occupations does not show that it affects chiefly persons with a high nervous organization, who are correspondingly reactive to nervous and psychic stimuli.

Allergic phenomena are considered an important etiologic factor, and in many cases it is believed that the primary symptom—pruritus—is itself an expression of allergy.

Local trauma, usually minimal but regularly repeated over a long time, is believed to be the chief single factor in the etiology. This may arise from such circumstances in the environment as friction, scratching,

rubbing or pressure from clothing or in association with various postures or movements connected with occupation, or it may be produced by the patient's activities in response to pruritus arising from internal causes. In any event, a habit of rubbing and scratching is acquired. In susceptible persons this in turn produces definite structural changes in the skin, which are indicated by visible alterations, such as thickening and pigmentation, and a local increased irritability. The latter change calls for further and more violent friction, which brings in response still more intense structural and functional reactions, completing the vicious circle.

The best single agency in therapy is the roentgen ray.

ABSTRACT OF DISCUSSION

Dr. Paul A. O'Leary, Rochester, Minn.: I am in accord with Dr. Cleveland's effort to revive the term lichen simplex chronicus, because I believe the terms neurodermatitis and neurodermitis have been greatly abused. When one uses the word neurodermitis, particularly in the literature, one usually encloses in parentheses the term one is trying to talk about, because neurodermitis has been used so loosely in this country and abroad in the discussion of different diseases. In other words, neurodermatitis has been so freely applied to atopic eczema and to diseases of psychic or neurogenic origin, as well as to the truly neurogenic diseases, that I am heartily in accord with Dr. Cleveland and think that he should be congratulated on endeavoring to reestablish the term lichen simplex chronicus.

It is rather hazardous to discuss pruritus ani as solely a neurogenic disease because of the established examples of the bacterial and mycotic origin of the condition and the various colonic diseases so common in the production of pruritus ani. The same idea is applicable to lichen planus, dermatitis herpetiformis, vitiligo and aphthous lesions of the mouth. I question that these conditions should be admitted to the group of neurogenic diseases.

Dr. Samuel M. Peck, New York: One must be careful in discussing eczema to differentiate three groups: first, the lichen simplex chronicus of Vidal; second, the neurodermatitis which may be limited to one patch or may assume a disseminated form, and, third, that type of eczema which becomes lichenified and is difficult to differentiate from the second group. Clinically, real neurodermatitis is characterized by a papule for the primary lesion, while lichenified eczema begins as a vesicular eruption. It is important to differentiate the three groups, because probably there is some difference in the underlying mechanism.

Dr. Samuel Goldblatt, Cincinnati: I was interested in Dr. Cleveland's statistics on the incidence of neurodermatitis in various races. I wish to call attention to the fact that in over 20,000 Negroes examined I have seen a case in only 1, a young girl. That does not seem to coincide with the theory presented here.

Dr. W. U. Rutledge, Louisville: In view of the fact that Dr. Cleveland's paper will ultimately get into the hands of a number of general practitioners and because in the last six weeks I have had 2 patients with lichen simplex chronicus, 1 of whom had come under the treatment of a surgeon and the other of a general practitioner with an x-ray machine, I think it wise to stress that the ultimate and the most satisfactory method of treatment in cases of lichen simplex chronicus is to find out the one or more etiologic causes and not

to stress the use of roentgen rays in effecting a cure. Both my patients had received second degree burns as the result of protracted and uncontrolled roentgen treatment, and the results of the treatment were far worse than the effects of the original condition. For that reason I think it wise to emphasize and reemphasize the danger associated with the administration of roentgen rays in the treatment of this condition.

DR. D. E. H. CLEVELAND, Vancouver, B. C.: Other papers have confirmed my original idea that lichen simplex chronicus is identical with the dry type of so-called neurodermatosis or neurodermatitis.

Dr. Peck stressed the distinction between lichenified eczema and lichen simplex chronicus. I have endeavored consistently to do this. I always question the patient about moisture; unless moisture is distinctly due to trauma produced by the patient, excoriations and digital attacks, I consider the eruption to be dry, neurodermatitis and lichen simplex chronicus.

I have tried to give full consideration to the allergic factor, as I think I have made clear.

With reference to Dr. Goldblatt's remarks about his Negro patients with lichen simplex chronicus, my experience has been almost opposite to his. Fifty per cent of my Negro patients have had lichen simplex chronicus, and I have had only 2 Negro patients. I agree with Dr. Rutledge's strictures on my advocacy of the use of roentgen rays. When I spoke of roentgen rays as being the best treatment for the lesions it was to be understood that I meant in the hands of a capable roentgenologist. Unfortunately there are persons everywhere who play with roentgen rays. That is important and cannot be too greatly stressed. I do not know of any other form of treatment that will cause improvement in well developed lichen simplex chronicus.

PSORIASIS

A BRIEF HISTORICAL REVIEW

PAUL E. BECHET, M.D.
NEW YORK

Psoriasis is an antidote for dermatologists' ego. It is the most vulnerable point in their armor as experts, and it remains the most baffling of dermatoses despite the great advances recently made in dermatology. Dermatologists of today can ill afford to look askance at the masters of yesterday, for except in diagnosis and palliative treatment they have accomplished nothing in the management of this disease.

Because of its antiquity, its confusion with leprosy and other dermatoses and the complete lack of progress both in its therapeutics and in the knowledge of its pathogenesis, the disease is of extraordinary interest, historically as well as philosophically. There is scarcely a therapeutic measure or an etiologic factor mentioned today which did not originate in the minds of dermatologists seventy or more years ago. It is passing strange that this apparent checkmate should have occurred in this particular disease. When one considers the advances in the treatment of syphilis in the past sixty years, it causes somewhat of a shock to realize that the use of chrysarobin, still a trump card in the treatment of psoriasis, was equally so as long ago as 1878.

Owing to its confusion with other dermatoses, many of the modern, as well as the ancient, writers have presented a maze of contradictory facts, which add greatly to the difficulty of correctly expounding their views. Pusey quoted that great French surgeon of the thirteenth century Henri de Mondeville as follows: "One calls serpigo, what the other calls impetigo, and the third pannus, a fourth places two diseases under one species and wishes to institute only one treatment for the two, while a fifth one divides impetigo alone into three species and establishes three different methods of treatment."

PSORIASIS OF THE ANCIENTS

Psoriasis is so striking a manifestation that it is hard to believe that it escaped the observation of Hippocrates and his celebrated school. Yet they described nothing that could definitely pass for it. They did, however, under the term *psora* describe a pustular disease which, in the opinion of Rayer,[1] corresponds to the present interpretation of impetigo.

Read at the Fifty-Eighth Annual Meeting of the American Dermatological Association, Inc., White Sulphur Springs, W. Va., May 2, 1935.

1. Rayer, P.: Treatises on the Diseases of the Skin, ed. 2, London, J. B. Baillière, 1835, p. 642.

According to Howard Fox,[2] the followers of Hippocrates grouped the dry, scaly eruptions under the term *lopoi* (from *lopos,* the epidermis, and *lepo,* to scale). This group probably included lepra, psoriasis, lichen and pityriasis, but no actual description of psoriasis was attempted.

Pusey,[3] in his delightful and erudite monograph on the history of dermatology, rightly ascribed to Celsus the credit for the first recognizable description of psoriasis. It is extremely fortunate for us that it should so happen that the only work extant of this remarkable genius is his "De re medica."[4] Chapter 28, in the fifth book of his work, included the first concise description of many cutaneous diseases, among which psoriasis can easily be identified.

Little is known of Celsus. He was born about 25 B. C. and died about 45 A. D. Despite his remarkable medical knowledge, it is doubtful that he ever practiced medicine. Pliny, according to Robinson,[5] named him among the *auctores* instead of among the *medici.* Sandys[6] expressed the belief that he was a Roman patrician who, like Cato, looked after the medical needs of his own family and slaves. The work of Celsus was not mentioned by ancient writers although Columella[7] in his "De re rustica" quoted him with great deference, as did also Quintilian[8] and Pliny.

Celsus described psoriasis under the heading of impetigo as follows: "The second species of impetigo is not unlike the papula, but of greater asperity and a more ruddy color, having various figures; scales fall off from the surface of the skin, there is a greater erosion, it spreads more quickly, and broader and both comes and goes at more certain intervals than the former. It is called the red." Under the heading of vitiligo he stated: "It is called alphos when it is white. It is commonly a little rough and not continued, but appears like drops dispersed here and there. Sometimes it spreads wider, leaving some places between free. The alphos comes and goes in some people without any regularity." These paragraphs of Celsus enable any one to recognize psoriasis, and,

2. Fox, Howard: Dermatology of the Ancients, J. A. M. A. **65**:469 (Aug. 7) 1915.

3. Pusey, W. A.: The History of Dermatology, Springfield, Ill., Charles C. Thomas, Publisher, 1933, p. 28.

4. Celsus, Aurelius Cornelius: De re medica, translated by James Greive, ed. 3, London, E. Portwine, 1837.

5. Robinson, Victor: The Story of Medicine, New York, Albert & Charles Boni, 1931, p. 98.

6. Sandys, John E.: A Companion to Latin Studies, ed. 3, London, Cambridge University Press, 1929, p. 718.

7. Columella: De re rustica, book 11, chap. 2.

8. Quintilian: Institutio oratoria, book 12, chap. 2.

as Hebra [9] pointed out, no succeeding work, even centuries later, has contained any better description of the disease.

It is perfectly true that the early Roman physicians produced little work of their own but depended greatly on the teachings of the abler Greeks, and Celsus was no exception to the rule. His work is a compendium of Greek medicine for Latin readers. His references to the works of Hippocrates, the parallel passages collected from Greek writings, the frequent use of Greek medical terms and quotations from the Alexandrian physicians along with the works of such members of the methodic school as Asclepiades and Themison all point to this conclusion.[10] On the other hand, Celsus made many original observations, especially along dermatologic lines.

Part of the manuscript of "De re medica" was discovered by Beccadelli at Siena in 1429 and anôther part by Thomas of Sarzana (Nicholas V) at Milan in 1443. The editio princeps was published at Florence in 1478 and soon became the most widely read textbook of medicine in Europe.

Galen (133 to 200 A. D.) was credited by Robert Willan [11] as the first to use the word psoriasis. Galen applied the term to a scaliness of the eyelids and corners of the eyes and to a rough and scaly state of the scrotum, attended with great itching and much excoriation. The concept is entirely different from that of psoriasis.

Owing to its indiscriminate use in the Old Testament, the word lepra covers other dermatoses, such as ichthyosis, elephantiasis, vitiligo and psoriasis. The latter, therefore, was never definitely described by the ancient Hebrews. The year 476 A. D. witnessed the fall of the Roman Empire, and with the exception of the work of the Byzantine and Arabian writers, who, though brilliant men, did not identify psoriasis, medicine began to feel the blighting influence of the approaching dark ages.

PSORIASIS OF THE MIDDLE AND MODERN AGES

Hebra [9] ascribed the paucity of original observation in the middle ages to the fact that the writers of that period spent all their time in frivolous commentaries on the works of the Greek and Roman masters and none on clinical observation. Not a single book from the fifth to the nineteenth century contained a better description of psoriasis than did that of Celsus. Neither Lorry nor Plenck gave an accurate account

9. Hebra, Ferdinand: On Diseases of the Skin Including the Exanthemata, translated by C. Hilton Fagge and P. H. Pye-Smith, London, New Sydenham Society, 1868, vol. 2, p. 3.

10. Le Clerc, Daniel: Histoire de la médecine, Amsterdam, G. Gallet, 1702, pt. 2, book 14, sect. 11, chap. 4, p. 219.

11. Willan, Robert: On Cutaneous Diseases, Philadelphia, Kimber & Conrad, 1809, vol. 1, p. 115.

of this common disease. Of course that was, in the main, due to the fact that leprosy, elephantiasis, vitiligo, ichthyosis, tuberculosis cutis, impetigo and even scabies were not differentiated by the medieval authors but were considered different forms of leprosy.

Perhaps thousands of persons with psoriasis during the greatest prevalence of leprosy, from 1000 to 1400 A. D., received the same brutal treatment as did real lepers, who were forced to carry a bell or clapper to warn the healthy from their path, wore a special dress, were not allowed to talk above a whisper to a healthy person and could not touch any one with their hands or eat with any one other than a leper. The Church performed the burial service over them, and they were declared officially dead. They were even ordered burned at the stake by Philip the Fair of France in 1313. How many patients with psoriasis suffered the horrible fate of real lepers is conjectural, but in view of the fact of the confusion of the disease with leprosy for so many centuries, it must be admitted that it is most plausible that many cases of error occurred. This confusion between the two diseases lasted for almost nineteen centuries, an incredibly long time.

Robert Willan was the first to differentiate partially between the two, and he also for the first time gave the disease the name psoriasis, a name unused since Galen mentioned it to describe an entirely different dermatosis. Willan, moreover, deserves the credit for being the first to consider psoriasis as a clinical entity and to describe its varieties fully. Unfortunately he was too greatly influenced by the ancient writers and could not completely eliminate leprosy as an associate disease, for under the designation "lepra vulgaris" he gave a typical description of psoriasis.

According to Besnier, Brocq and Jacquet,[12] Willan's great French contemporary Alibert did not seem to have the least understanding of psoriasis. He vaguely described the disease under the names *dartre sèche, dartre squameuse lichénoide* and *dartre furfuracée.* Alibert[13] used the term *psoride pustuleuse* as a synonym for scabies.

The English dermatologists, Tilbury Fox,[14] Neligan,[15] Gaskoin,[16] Thomson and Parkes used the term lepra vulgaris to describe psoriasis.

---

12. Besnier, Ernest; Brocq, L., and Jacquet, L.: La practique dermatologique, Paris, Masson & Cie, 1904, p. 88.

13. Alibert, J. L.: Description des maladies de la peau observées à l'Hôpital Saint Louis, et exposition des meilleures méthodes suivies pour leur traitement, ed. 2, Bruxelles, A. Wahlen, 1825, vol. 2, p. 563.

14. Fox, W. T.: Skin Diseases: Their Description, Pathology, Diagnosis and Treatment, second American edition from the London third edition, New York, William Wood & Company, 1873.

15. Neligan, J. M.: A Practical Treatise on Diseases of the Skin, Dublin, Fannin & Co., 1866, p. 230.

16. Gaskoin, George: On the Psoriasis or Lepra, London, J. & A. Churchill, 1875.

According to Nobl,[17] Erasmus Wilson used the name psoriasis for squamous eczema and the name alphos as the correct designation for psoriasis.

The Frenchmen, Biett, Rayer, Cazenave and Devergie also confused the two diseases. Hebra, in 1841, was the first to eliminate the word lepra in the consideration of psoriasis, and, for all time, he gave a complete scientific conception of the latter disease. On the other hand, it is only fair to note that Gibert [18] one year earlier stated that in his opinion lepra vulgaris was only another variety of psoriasis.

For those inclined to smile at the vagaries and confusion of their immediate predecessors, I should like to call attention to the fact that Abramowitz [19] presented a case before the Section on Dermatology and Syphilis of the New York Academy of Medicine on Oct. 6, 1925, for differential diagnosis between leprosy and psoriasis, which neither he, Pollitzer nor Wise could determine, and also that Sutton [20] and Ormsby [21] in their textbooks still used the old confusing terms lepra and alphos as synonyms for psoriasis. Stelwagon was more canny, as after the words lepra and alphos he added in parenthesis "of old authors."

THE THERAPY OF PSORIASIS

Probably the earliest therapy of psoriasis was that described in the Papyrus Ebers,[22] written about 1500 B. C. Such local remedies as cat's dung, dog's dung and berries of the xet plant were recommended for the scurf. To drive away leprous spots on the skin a mixture of onions, sea salt and urine was recommended. For "scabs in every limb" a mixture of "fresh oil, goose oil and semen" was said to be efficacious. If this failed one might try "wasp's dung in milk of the sycamore." After the scales had been removed, an excellent application was "scribe's excrement mixed thoroughly in fresh milk and applied as a poultice." It is with relief that one turns from these scatologic remedies to the red nitre and sulfur recommended by Celsus fifteen hundred years later.

17. Nobl, Gabor, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 7, pt. 1, p. 180.

18. Gibert, C. M.: Traité pratique des maladies spéciales de la peau, ed. 2, Paris, Germer-Baillière, 1840, p. 323.

19. Abramowitz, E. W.: Leprosy? Psoriasis? Case Presentation, Arch. Dermat. & Syph. **13**:276 (Feb.) 1926.

20. Sutton, Richard L.: Diseases of the Skin, ed. 6, St. Louis, C. V. Mosby Company, 1926, p. 208.

21. Ormsby, Oliver S.: A Practical Treatise on Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1927, p. 259.

22. Bryan, Cyril P.: The Papyrus Ebers, New York, D. Appleton & Company, 1931.

Galen enlarged on the benefit of a broth in which a viper had been boiled, and it is an indication of the complete therapeutic stagnation throughout the centuries that the same remedy was recommended by Daniel Turner [23] in 1723. This author [24] related in detail the therapy pursued in the case of a young woman suffering from nummular psoriasis with lesions on the face, elbows and knees. The therapy consisted of thorough inunction of mercurial ointment for the purpose of inducing salivation. Mercurialism occurred on the third day. Turner described it as follows: "Her mouth was stiff and hot. Her belly produced several stools, with perpetual tenesmus. The last stool contained much mucus from the guts, with some sprinkling of blood." The day after another inunction, a few days later, he "found her very dull, her gums inflamed and tumid, and her mouth began to stink. She was retching and had spit from the morning about three quarters of a pint." A day later 20 grains (1.3 Gm.) of mild mercurous chloride was administered, and twenty-four hours later another dose of 30 grains (1.9 Gm.) was given. Later in the day the gums were so swollen that the teeth were entirely covered. On visiting her the next day Turner stated: "I smelt as encouraging a stink from her mouth as could be wished for." On the following day more mild mercurous chloride was given, and an excoriating application was made to the swollen oral mucous membrane in order to keep the salivary ducts open. As the patient did not expectorate more than a pint a day, it was decided to desist from any further salivation and to make up the deficiency by sweating and purging.

Despite these efforts new spots appeared, "The distemper still budding and manifesting its perverse nature," wrote Turner. A second case reported by the same author showed considerable improvement after the patient had consumed forty vipers, first eating the flesh and then drinking the broth in which they were boiled.

In view of this ghastly therapy, it is a curious anomaly that Turner was apparently the first to use ammoniated mercury ointment in the local treatment of psoriasis. The ointment is still widely used at the present time, two hundred and twelve years later.

Chrysarobin, probably the best local remedy in use at the present time, especially for inveterate psoriasis, was introduced by Balmanno Squire [25] in 1876. Chrysarobin, previously used for a long time in India as a cure for ringworm, came originally from Bahia, a province in the Empire of Brazil. It was soon imported in Goa, a Portuguese

23. Turner, Daniel: A Treatise of Diseases Incident to the Skin, ed. 2, London, R. Bonwicke, 1723, p. 18.

24. Turner,[23] p. 32.

25. Squire, A. J. B.: On the Treatment of Psoriasis by an Ointment of Chrysophanic Acid, London, J. & A. Churchill, 1878, p. 8.

colony on the west coast of Hindustan; hence its name "Goa powder." In Brazil the drug was known as Araroba powder, and in the Malay peninsula, and Cochin China as *Poh di Bahia,* or Bahia powder. Its effectiveness in the treatment of ringworm in the East made it very popular. It is interesting to note that Squire's discovery of its beneficial effect on psoriasis was entirely due to the fact that one of his patients, with chronic psoriasis, while residing in China had on his own initiative caused patches of the disease to disappear by means of its local application, and it was on this patient's recommendation that Squire began its use. Little did he know at the time that seventy-nine years later it would remain in almost universal use.

Arsenic for the treatment of psoriasis still has a fairly large number of devotees, certainly not nearly as enthusiastic as they formerly were but still sufficiently voluble to command much space in the sections on the therapy of psoriasis in modern textbooks. Solution of potassium arsenite is still the perennial favorite. Its originator, Thomas Fowler, was a pharmacist as well as a physician and was a most able man. His famous "mineral solution" (solution of potassium arsenite) was introduced in 1786, and, strange to say, its first use was in the treatment of malarial fever.[26]

The first mention of the use of arsenic in the treatment of psoriasis was in an article by Thomas Girdlestone,[27] in which he reported its successful use in psoriasis. Girdlestone preached assiduously against excessive dosage; his average dose was 6 drops three times a day, and his largest, 12 drops, which he rarely used.

Dr. Brown, a contemporary of Girdlestone, a member of the Royal College of Physicians and senior physician to the Infirmary at Margate, made frequent use of a solution of potassium arsenite in psoriasis. The remedy soon became immensely popular in combating the disease. It was used orally until 1869, when E. Lipp [8] for the first time injected it subcutaneously, using a solution of arsenous acid.

Hebra seems to be responsible for the "Asiatic pill," which he highly recommended. His original formula called for 66 grains (4.22 Gm.) of arsenous acid and 9 drachms (34.9 Gm.) of powdered black pepper with acacia and water, so as to make 800 pills. Each pill contained 0.0825 grain (52.8 mg.) of arsenous acid. From 3 to 12 pills were administered daily, until the entire 800 were taken. Hebra's successor, Kaposi, also contributed greatly to their vogue in Europe.

---

26. Bechet, Paul E.: Arsenic: History of Its Use in Dermatology, Arch. Dermat. & Syph. **23**:110 (Jan.) 1931.

27. Girdlestone, Thomas: Observations on the Effects of Dr. Fowler's Mineral Solution in Lepra and Other Diseases, London M. & Phys. J. **15**:297 (April) 1806.

28. Lipp, E.: Arch. f. Dermat. u. Syph. **1**:362, 1869.

According to MacKee [29] roentgenotherapy for psoriasis began in 1900. Among the first to use this modality in Europe were Strater, Hahn, Albers-Schönberg and Startin, and in this country, Pusey, Williams, Morton, Allen and Zeisler. It has unfortunately not resulted in a single cure, despite its great value in temporarily removing patches of the disease.

A list of all the remedies for psoriasis which have appeared on the therapeutic stage, taken a bow and made an exit would only be boring and most discouraging. Suffice it to say that this dermatologic bête noire is still a complete etiologic and therapeutic enigma, despite its long association with man and its careful study.

Let it be hoped that the increasing enthusiasm in the ranks of dermatologists may soon result in the discovery of the cause of the disease and its subsequent elimination, and with that hope, I close this effort to summarize these few historical facts on psoriasis.

ABSTRACT OF DISCUSSION

Dr. William Allen Pusey, Chicago: I am obliged to Dr. Bechet for his paper. I think he has been happy in selecting psoriasis for a historical topic. Its history is most interesting. There is a good deal to be gained by such excursions into the past. I thought I saw a tendency in some of the discussions here for dermatologists to feel cocksure of themselves, and I know nothing that will check this or make one feel more tolerant of the views of other people than the consideration of such a disease as psoriasis. I can visualize some historian two or three hundred years from now reviewing the discussions of today as to whether some little things shall be called tags or papillomas, or whether a condition shall be called sarcoid, which has a significance of malignancy, and wondering how in earlier years their colleagues could have been so stupid. And when it comes to discussions of eczema, seborrheic dermatitis and the separation of these conditions from scabies, a good laugh will go around. As a matter of fact, physicians are the result of their times, and I know of nothing that will do more to relieve their views than such papers as Dr. Bechet's.

Dr. George Miller MacKee, New York: Dr. Bechet has given an excellent presentation of historical value. Historical contributions are both interesting and valuable. At times one is impatient with them because one is busy with things that seem more important. Knowledge is largely the result of the work of one's predecessors, and, as Dr. Pusey said, recognition of the work of past masters causes a becoming and useful spirit of humility. I venture to say that few of the younger men have any idea of the difficulties encountered by the pioneer roentgenologists, yet it is their work that makes roentgen ray work so easy today. I think that historical dermatology is so important, particularly to young men coming into the field of dermatology, that I have added to my curriculum a course in historical dermatology.

---

29. MacKee, George M.: X-Rays and Radium in the Treatment of Diseases of the Skin, ed. 2, Philadelphia, Lea & Febiger, 1927, p. 517.

INCIDENCE OF DERMATOPHYTOSIS AT THE BOSTON CITY HOSPITAL

JOHN W. WILLIAMS, M.D.
CAMBRIDGE, MASS.

About a year ago the idea was conceived that some valuable information might be stored in the clinical histories of cases of dermatophytosis of the dermatologic department of the dispensary of the Boston City Hospital. While some persons may maintain that no study of dermatophytosis should be made on records of cases unaccompanied by microscopic and cultural examination, my opinion is that if one is to have an ample record of this clinical entity in years past one must have numbers of cases, and if one is to have numbers one will not find records of cases with microscopic and cultural examinations. However, one can find numerous records of cases in which the patient was examined and the condition was diagnosed by a dermatologist of many years' experience, whose ability is unquestioned. True, there are summaries of cases observed in private and clinical practice which are accompanied by microscopic and cultural examination, but the numbers are probably too small for one to draw sufficient definite conclusions. Therefore, two courses are open: to use the records of cases accompanied by microscopic or cultural observations or to use the larger number of records of cases in which the condition was diagnosed by an expert. I have chosen the latter course and believe that the study and enumerations warrant due consideration.

I do not deny that histories recorded in the clinics of large hospitals are taken under stress. Often there are omissions and occasionally mistakes. However, I am of the opinion that dermatologists frequently underrate the value of the clinic history. I have attempted to omit cases when the history or portions of the history are questionable. Since the summary begins in 1926, when a diagnosis of dermatophytosis or a condition now considered synonymous was not as frequently made, the report is probably less accurate for earlier years.

In the report I have considered the following points: (1) race, (2) monthly and yearly incidence, (3) sex, (4) age, (5) occupation, (6) site of involvement, (7) chronicity and (8) associated disease or injury.

Contribution no. 63 from the Department of Biology and Public Health, Massachusetts Institute of Technology.

From the Homberg Memorial Infirmary and the Department of Biology and Public Health, Massachusetts Institute of Technology.

METHODS

In the presentation of the material I have resorted to three charts, in order to conserve space and make for clarity. In chart 1 along the ordinates are plotted the cumulative numbers of cases. The figure 1 in the margin near the bottom of the chart designates 10 cases; the figure 1 above, 100 cases, and the next figure 1 represents 1,000 cases. To the other figures are added zeros corresponding to the 1 immediately below. Years are plotted along the abscissas. Visits to the hospital and new and return visits to the clinic, as indicated by the curves, must be multiplied by 10, since it was necessary to divide the number of the visits by 10 to include them in the chart. The structure of chart 2 is similar to that of chart 1, except that the groups are plotted according to age on the abscissas; the population of Boston plotted according to age groups is divided by 10.

Chart 3 is a contour graph [1] by which three factors have been plotted, with cumulative numbers of cases along the ordinates, years along the abscissas and sites of involvement according to sex on the chart.

OBSERVATIONS

Race.—Two races are represented, white and Negro. Three and fifty-eight-hundredths per cent of the patients were Negro, and the remainder were white. According to the 1930 census for Boston, 2.64 per cent of the population was Negro. This would indicate that Negroes are at least proportionally as susceptible as members of the white race. Living conditions and the financial status, which are usually comparatively lower with Negroes, and greater freedom from restraint toward free service might make them less hesitant in patronizing a free dispensary. Prevalence of the flatfoot and obesity among the women of this group should be considered. In the summaries, the cases of Negroes are included with those of the white patients, since the cases studied bore no distinctly different characteristics and were not of sufficient number for individual analysis.

Monthly and Yearly Incidence.—Many factors might contribute to the increase in visits to a dermatologic clinic in a free dispensary for treatment of this disease in the last eight years. Consciousness of the disease on the part of the public and of the medical profession owing to advertisements and publications, would increase awareness of its existence. This factor would result in an increase not only in the number of new cases recognized but also in the number of referred cases. In the earlier years a lack of knowledge of the potential seriousness of the disease and its novelty would be contributory. Later, realization of the chronicity of the disease on the part of many would discourage the payment of repeated fees to physicians in private practice and would encourage gravitation to the free clinic. Idleness caused by the depression would, owing to necessity and to the time available to attend, increase

1. Williams, John W.: The "Contour" Chart and Its Importance in Public Health Tabulations, Science **82**:425 (Nov. 1) 1935.

the number of visits. An increased sale of second-hand apparel and a decrease in purchases of new clothing might also contribute.

In chart 1 the trend of the disease is compared with the number of new visits to the clinic, the number of return visits to the clinic and the total number of visits to the hospital. It will be noted that the number of cases among men was higher than that among women except during 1927. A part at least of this difference was due to the proportionately

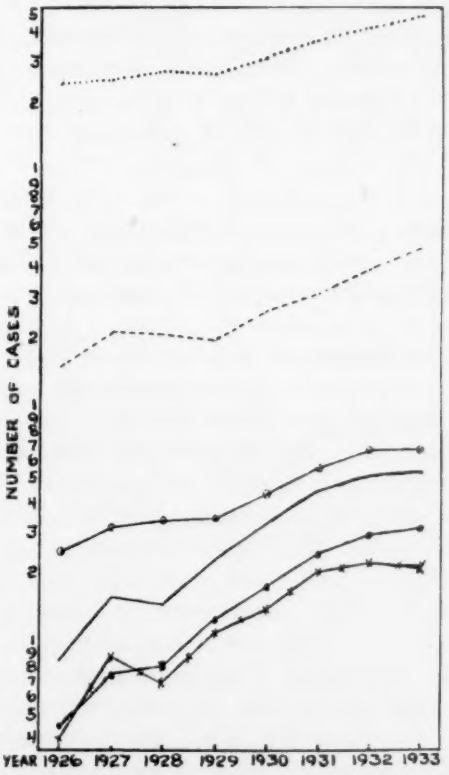

Chart 1.—Incidence of dermatophytosis from 1926 to 1933. The dotted line represents the total number of visits to the hospital; the dashes, the number of return visits to the clinic; the solid line with open circles, the number of new visits to the clinic; the solid line, the total number of cases in both sexes; the solid line with stars, the incidence in women, and the solid line with solid dots, the incidence in men. The 1 along the left-hand margin near the bottom of the chart designates 10 cases, the 1 above, 100 cases, and the next one, 1,000 cases. The total number of visits to the hospital and the number of new and return visits to the clinic must be multiplied by 10.

increased number of cases in which women's fingers were affected. Following this increase there was a decrease in 1928. The decreases affected women more than men, and in this instance there was a pro-

portionately greater decrease in cases involving both the hands and the feet in women. It occurred to me that the advent of rayon, which is a poorer culture medium for some fungi than the other materials used in socks and stockings, might play a rôle. This idea, however, was soon discarded, since rayon at this time was used to a greater extent in men's hose and since the increase in the number of cases in men in the succeeding years was marked. I found no change in the materials used in shoes at this time, nor did I note any unusual variation in the humidity or temperature.

It is apparent from chart 1 that all the curves have the same trend. In the first four years the increase in dermatophytosis seems out of proportion to the increase in new and return visits to the clinic and total visits to the hospital. In the last four years, however, this increase was not out of proportion. In the years 1932 and 1933 there was a slight proportionate decrease over return visits to the clinic and total visits to the hospital. In order to substantiate further the results shown in chart 1, a twelve month moving average centered at the fifteenth of the month was charted for the period. The trend corresponded to that shown in chart 1.

Data similar to those shown in chart 1 were charted with the months of the year instead of with the years. The variations noted were more marked for women, the lowest incidence appearing in December, with only a few more cases in February and September and slightly more in January. The highest incidence for women was in August. For men, the lowest incidence was in February, with only a few more cases in January and December. The higher incidence for men was distributed over the months of May, June, July and August. The December depression, which was more pronounced for women, might be explained by the holidays, when visits for minor ailments are postponed until later. The severe weather and fewer days of February might account for fewer cases in that month. The depression noted for women in September is not accounted for unless the high point during August resulted in some immunity. The difference between the lowest and the highest monthly incidence for women was 59 per cent (77 cases) and for men, 43 per cent (60 cases).

Sex.—Many factors are to be considered in the study of the incidence of dermatophytosis according to sex, such as habits, wearing-apparel, occupation, site of involvement and exposure. The female sex has been characterized as being the more cleanly. In general, women's wearing-apparel tends toward better aeration and a smaller accumulation of perspiration. The shoes, for example, are not of the confining and bunglesome type worn by men; women's feet are small, and their stockings are usually of a lighter weight. Women's vanity compels them to

pay attention to both the feet and the hands. Their occupations as a rule are not as strenuous and their contacts are not as close as those of men.

It will be noted in the charts that curves are given for men and for women. There was not as great a difference in the number of cases as one might expect. There was a difference, however, in the site of involvement, in that women were more prone to involvement of the hands, and men were more prone to involvement of the feet. There are three possible explanations: 1. A woman has a daintier skin and at work with the hands might be more prone to injury. 2. She uses chemicals in the toilet of her nails and subjects them to much manipulation. 3. She washes dishes and garments. The latter would encourage one to look to laundries for a number of cases. Inquiry in Boston, however, has been unsuccessful in disclosing increased incidence in laundries.

Age.—In this study I have considered cases by age groups of 5 years. Naturally one would expect increased incidence during the periods of life of increased contact with the outer world. In order to appreciate the incidence, I have included in chart 2, five year age groups interpolated from the Massachusetts census of the unemployed of Jan. 2, 1934. Each point plotted represents the number of cases in the five year group directly preceding. If one takes, for example, the age group from 16 to 20 years, one sees that there were 300 patients to 63,000 persons and that 140 patients were women and 160 men. By comparison one notes great prevalence of the disease in both sexes between the ages of 16 and 60 years. There is an increase in incidence in the group from 46 to 50 years in women, and I am reminded of changes at the menopause and the numerous associated disturbances.

Studies were made of the curves according to age for men and women and of the totals for the individual years. Sharp peaks were noted for the group from 21 to 35 years in 1930, 1931 and 1932, but the peak for 1931 was especially pronounced. Irregular peaks were present in the remainder of the years studied.

When a chart was plotted, using cumulative numbers of cases for the ordinates, years or months for the abscissas and age groups on the chart, the distribution for the several years and months was approximately proportionate to the distribution in age groups of the population between 16 and 60. This indicates that no age group was selectively involved in the different months of the year or in the different years studied. It also indicates a lack of immunity, since if immunity were developed the proportionate number of cases for the age group would be less. In the early years of life there are fewer cases, possibly because of less exposure to the causative agent. In later years, it is probable that the patient is less ambulatory and so is less likely to patronize the clinic. The foregoing observations apply to both men and women. One gains the

impression from the literature that persons of high school and college age are more likely to be infected, but I have no evidence to this effect.

Occupation.—I have attempted to study the relation of the site of lesions in respect to the occupation of the patient. Unfortunately, the

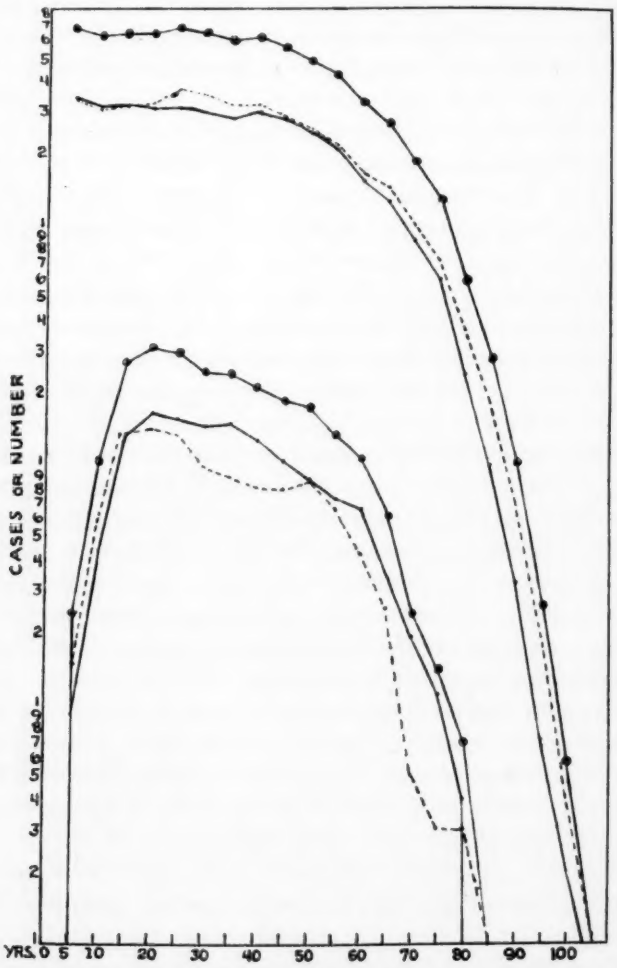

Chart 2.—The incidence of dermatophytosis according to age. The upper group of curves represents the age groups (in five year periods) of the population of Boston according to the census of Jan. 2, 1934. The number as indicated by the curves should be multiplied by 10. The lower group of curves indicates the incidence of dermatophytosis from 1926 to 1933 inclusive. The broken line represents females; the unbroken line, males, and the line with solid dots, the total number of cases.

number of patients with similar occupations was limited. One would expect that persons who were on their feet excessively and who used

their hands only moderately might suffer from the disease on their feet. Indefiniteness of the duties, as indicated by the occupation, however, prevents me from drawing definite conclusions.

I am not attempting to discuss dermatophytosis from the standpoint of dermatophytids or from the standpoint of irritation of an area and localization there of the organism, with resultant lesions, as was ably demonstrated [2] in rabbits after scarification and intravenous injection of Trichophyton gypseum. I believe that irritation may be a factor in localization whether the resultant lesion is classified as dermatophytid or dermatophytosis.

The tabulation indicates that there are comparatively few occupations in which there is an excess of cases involving the hands over those involving the feet. Women working as stenographers, telephone operators, nurses, saleswomen and operators in beauty parlors had a greater incidence of involvement of the hands. A few classes of workers part of whom are men and part women such as restaurant workers, inspectors and teachers, also showed a slight excess of cases of involvement of the hands. The only male workers showing an excess of cases of involvement of the hands were tailors, mechanics, masons and pedlers. The greatest number of cases of involvement of the hands and feet was registered among policemen, and the greatest number of cases of involvement of the body occurred among stenographers. Laborers, chauffeurs, salesmen, firemen, tailors, meat-cutters and junkmen led the list in involvement of the groin.

In the tabulation involvement of the body is recorded for patients who did not show involvement of the hands, feet or groin. In some cases there were additional sites of involvement, which will be discussed later.

Occupation	Hands	Feet	Hands and Feet	Body	Groin
Artist	0	0	1	1	0
Baker	8	8	0	0	1
Barber	2	6	0	0	2
Beauty operator	3	0	1	0	0
Bindery worker	2	2	0	0	0
Blacksmith	0	3	0	0	0
Bottler	1	0	0	0	1
Candy maker	2	2	0	0	0
Carman	0	2	0	0	0
Carpenter	4	12	2	0	1
Chauffeur	9	16	4	1	4
Cleaner	2	1	0	0	1
Clerk	9	25	4	0	1
Collector	1	1	0	0	1
Contractor	1	0	0	1	0
Cook	4	4	3	1	1
Custodian	11	15	2	0	1
Cutter	0	2	1	0	0
Draftsman	0	1	0	0	1
Elevator operator	1	1	0	0	0
Engineer	1	3	1	0	0

2. Fried, S. M., and Segal, M. B.: The Hematogenous Production of Dermatomycoses: Experimental Studies, Arch. Dermat. & Syph. **19**:98 (Jan.) 1929.

Occupation	Hands	Feet	Hands and Feet	Body	Groin
Errand boy	0	7	0	2	0
Finisher	1	0	0	0	1
Fireman	4	16	2	0	4
Foreman	1	2	1	0	1
Garment worker	6	7	0	3	0
Gas worker	0	6	0	0	0
Inspector	5	4	2	1	1
Iron-worker	1	2	0	0	1
Junkman	0	1	0	0	3
Laborer	25	70	10	0	17
Lathe hand	1	0	0	1	0
Laundry worker	3	3	1	0	0
Longshoreman	1	1	0	0	0
Machinist	2	4	2	1	2
Maid	1	3	0	2	0
Mail carrier	1	1	0	0	1
Mason	4	3	1	0	0
Meat cutter	2	7	1	0	3
Mechanic	5	4	1	0	0
Metal worker	0	2	0	0	1
Molder	0	3	0	1	1
Musician	1	1	0	0	1
Nurse	6	1	0	0	0
Operative	0	1	1	0	0
Orderly	0	2	0	0	0
Packer	1	3	0	0	1
Painter	7	12	0	2	2
Pedler	3	0	0	1	0
Physician	0	1	0	1	2
Pipe-fitter	1	1	0	0	0
Plumber	1	3	0	0	1
Policeman	4	9	5	1	0
Printer	4	6	2	0	1
Radio worker	1	0	1	0	0
Restaurant worker	13	12	2	0	1
Roofer	1	3	0	0	0
Saleslady	6	0	0	0	0
Salesman	9	16	4	2	3
Seaman	0	2	2	0	1
Shipper	4	4	3	0	2
Shoeworker	11	14	3	0	2
Steam-fitter	0	3	1	1	0
Stenographer	10	8	3	4	0
Stockman	0	3	0	0	0
Storeman	1	4	0	0	0
Tailor	9	8	4	0	5
Teacher	3	1	0	0	0
Teamster	0	2	0	1	0
Telegrapher	0	1	1	0	0
Telephone operator	6	2	0	0	0
Tinsmith	0	3	0	0	0
Upholsterer	1	0	1	0	1
Watch maker	0	0	2	0	0
Window cleaner	1	2	0	0	0

One person of each of the following occupations suffered from lesions on the hands: baggage master, bootblack, chemical worker, dishwasher, druggist, entertainer, farmer, floor layer, investigator, paver, piano maker, picture framer, poultry worker, service man, sprinkler fitter, tobacco worker and watchman.

One person of each of the following occupations had lesions on the feet: assembler, cap maker, cigar maker, compositor, engraver, fire alarm operator, fire extinguisher worker, fruit dealer, furniture mover, librarian, lithographer, marker, matron, mill worker, oil man, photograph finisher, plasterer, polisher, scale operator, sheet metal worker, sign writer, social worker, sugar worker, tile setter and valve tester.

One person of each of the following occupations had lesions on the hands and feet: boiler helper, boiler scaler, capmaker, florist, iceman, patent maker, sewer inspector, tester, treer and truck driver.

A box maker, a car cleaner, an electrician and a gardener had lesions on the body.

A meter reader, a pressman, a soldier, a sticker and a tool maker had lesions on the groin.

Occupations are given in alphabetical order, so as to insure ease of reference. It is realized that any arrangement of occupations without more specific information as to exact duties would be subject to criticism, and it is felt that a tabulation such as this can be taken only as a reference for others interested in this or a like problem.

Site of Involvement.—Variations of the extent and intensity of involvement in this disease are considerable. With reference to extent, I have listed cases under the headings hands, feet, hands and feet, body and groin. This list is confined to cases of involvement in these areas. Under body are placed cases of more extensive involvement than would be indicated by the other captions. Undoubtedly, involvement is often more extensive than is appreciated by the patient. Probably much itching on the body results from a bland irritation caused by the etiologic organism of epidermophytosis.

Sites included under the listing for the body with the hands were: body, 4 cases; face, 4; feet, body, 2; forearms, arms, 13; ankles, 2; feet, arms, 2; groins, 2; legs, 4; neck, 2 and each of the following, 1 case: arms, legs, body, face; body, extremities; elbow; face, body; face, legs; face, neck, buttocks; feet, axillae; feet, ears; feet, eyelids; feet, legs; feet, legs, ears; feet, legs, forearms; feet, thighs; forearms, face, neck; legs, arms; legs, popliteal spaces; thighs; scalp. Sites with the feet were: arms, legs, 2 cases; body, 4; groins, 4 and each of the following in 1 case: ankles, elbows; arms, anus; arms, legs; axillae, breasts, thighs, wrists; axillae, groins, legs; breast; buttocks, legs, face, chin, mouth; face; face, neck; forehead; forehead, groins; knees; neck, scalp; vulva and wrist. With hands and feet sites were: ankles, 9 cases; anus, 18; groins, 8; anus, vulva, 2; ankles, arms, 2; axillae, 15; axillae, groins, 3; buttocks, 5; face, neck, 2; leg, 24; popliteal space, 4; sacrum, 2; thighs, 8; wrists, 5 and each of the following in 1 case: axillae, cubital space; axillae, ears; axillae, legs; groins, back; groins, body; groins, popliteal space; groin, vagina; penis; thighs, ears; thighs, legs; vulva; vulva, forearms, body and each of the following in 1 case: antecubital areas; arms; arms, body; arms, elbows; arms, legs, trunk; body; breasts; cheeks; chest, abdomen; elbows; face; face, body; face, neck, back; forearms; knees; neck; neck, legs; nose; operation scar; tibial tubercles and wrists.

There were only a few histories in which antecedence of areas was given: involvement of feet following origin in the groins, 1 case; involvement in the groins following origin on the feet, 1 case; involvement of the hands following origin on the feet, 7 cases; involvement of the feet following origin on the hands, 4 cases; involvement of the feet following origin in the vulva, 1 case, and involvement of the scrotum following origin on the hands, 1 case.

On a study of chart 3 one is impressed by the prevalence of involvement of the hands among women and of the feet among men. In most instances this is reflected in the cumulative numbers of cases for the years and of the months. Of 1,819 cases of involvement of the hands and feet one notes the following distribution: on the hands, men 322 and women 498, and on the feet, men 644 and women 355. Previously I mentioned the possible factors in this occurrence. However, these

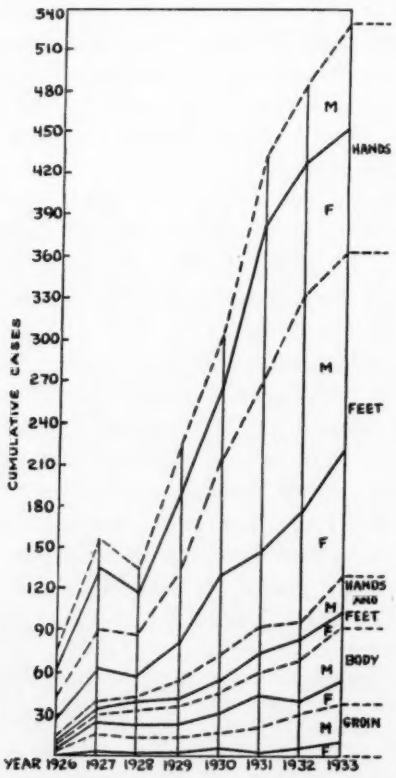

Chart 3.—The incidence of dermatophytosis according to the site of involvement.

factors do not explain the popular conception that involvement of the hands is of the order of a dermatophytid (allergic reaction) and secondary to involvement of the feet. If this were true one would find more cases of involvement of the feet, unless one is to assume that in a large number of cases of such involvement in women the condition of the feet is asymptomatic and goes unnoticed and that this is not true in men. This is of course possible; women, because of well aerated shoes, light stockings and better care of the feet, might have

foci without noticeable local signs but with distant allergic involvement in areas subjected to irritation. I see no reason that these foci should be confined to the feet were it not for perspiration, lack of aeration or uncleanliness. I see no reason why an allergic manifestation or epidermophytid might not be as prevalent on the feet as elsewhere or why many of the cases of symptomatic involvement of the feet might not result in part or entirely from an allergic reaction provoked by unnatural confinement, poor hygiene or irritation and proliferation of the foci. Thus, there might be asymptomatic foci, symptomatic foci and symptomatic allergic reactions in sensitized patients and asymptomatic and symptomatic foci in nonsensitive persons. Such reasoning would mean that any area (fingers) might be a focus or site from which the causative agent could be isolated. However, the probability of the feet being the focus would far exceed that of the other areas studied, since the apposition of the toes, the confined condition in which they are kept and their frequent greater neglect, deformity, poorer circulation, subjection to injury and greater change in temperature and weight would contribute to lowered resistance and provide an ideal focus for the dermatophyte. The fact that dermatophytes are recovered far oftener from the feet than elsewhere substantiates this assumption. The fact that many lesions of the feet yield fungi neither on microscopic examination nor on culture should raise the question of dermatophytid at this site. The tabulation and the foregoing reasoning leads me, therefore, to the conclusion that it is safer to consider the allergic reaction as a condition which may involve any area of the skin and even internal surfaces, as in cases of hay fever [3] and asthma.[4] In descriptions of lesions it might be better if more research and inquiry were directed toward the pathologic changes in the lesions from the standpoint of (*a*) lesions of sensitized skin, (*b*) lesions of unsensitized skin and (*c*) lesions embracing both reactions.

Further study of chart 3 reveals no appreciable variation in the sites of involvement for the years from 1926 to 1933. As will be noted, the interrupted lines separate the designated areas of involvement, and the uninterrupted lines, the men from the women. When a contour chart was plotted with months instead of years as the abscissas no significant variation of the site of involvement from month to month was noted. The cases of involvement of the groins were more common among men. Dirty occupation and lessened scrutiny with reference to cleanliness might well have contributed to this greater incidence.

When age groups are charted with reference to the site of involvement I find that up to 10 years of age the site of involvement in boys

3. Wise, Fred, and Sulzberger, Marion B.: Urticaria and Hay Fever Due to Trichophytin, J. A. M. A. **95**:1504 (Nov. 15) 1930.

4. Ramirez, M. A.: Trichophytin Sensitization, M. J. & Rec. **132**:382 (Oct. 15) 1930.

and girls corresponds. It is in the older groups that an excess of cases of involvement of the feet in men and of the hands in women is noted. This is to be expected, since it is after the age of 10 that the sexes become more distinguished. After 10 years of age the cases of the different sites of involvement are proportionately distributed in the different age groups.

Chronicity.—I realize that inquiry into the length of time the patient has had a disease is subject to one of the greatest of variables, memory. However, in a large group of cases I believe that some idea of chronicity might be gained. The shorter periods given should be fairly accurate and the longer periods less reliable. Also, since persons are inclined to think in terms of certain numerals, accuracy is impaired.

On the construction of a contour chart for the two sexes, using cumulative numbers of cases as the ordinates, sites of involvement as the abscissas and the length of the disease on the chart, the following information was obtained: The longest duration of the disease, in a case of involvement of the groins of a man aged 75, was given as forty years. Among women, there was history of duration of twenty years in 2 cases of involvement of the hands, in 1 of the feet, in 1 of the feet and hands and in 1 of the body. The youngest patient, with involvement of the genitals, was a girl aged 7 months. A boy of 10 months had involvement of the feet. The oldest patient, a woman of 90 years, had had involvement of the hands for eight years. A man of 78 had had involvement of the hands for eight years.

There was variation of chronicity with reference to the site of involvement. For example, the percentage of lesions in men of a duration of two months or less was as follows: feet, 64 per cent; hands, 49 per cent; hands and feet, 74 per cent; body, 58 per cent, and groins, 59 per cent. In women the percentages were: feet, 50; hands, 48; hands and feet, 59; body, 39, and groins, 27. Thus, in cases of involvement of the body and groins in women there was greater chronicity, and in cases of involvement of the feet and feet and hands in men there was least chronicity. This increased chronicity in women is hard to explain unless the habits mentioned previously play a part. It may be that the chronicity is more apparent than real, since a woman is more inclined to take account of conditions which threaten her beauty.

Associated Disease or Injury.—Since complete physical examination was not customary, I have been able to list only a limited number of associated diseases. In the order of their frequency they were: other cutaneous diseases, 86 cases; arthritis, 60; varicose veins, 38; obesity, 34; allergic conditions, 48; flatfoot, 24; injury, 20; diabetes, 9; hallux valgus, 7; gastric ulcer, 7; exposure to roentgen rays, 1, and an operative scar, 1.

SUMMARY

Data were collected from approximately 2,400 clinical histories of dermatophytosis, and material of interest and importance was tabulated.

In the arrangement of much of the data a chart arbitrarily called a contour chart was utilized. By means of this chart three factors can be recorded, such as months, cumulative numbers of cases and age groups.

The proportion of cases recorded for Negroes was slightly greater than that for white persons if the 1930 census for Boston is used in a comparison of the distribution among the white and the Negro population. The fact that the environs of the hospital are inhabited in large part by Negroes would lead one to believe that there would be a larger number of cases if Negroes were proportionately susceptible.

A decided upward trend in the disease occurred from 1926 to 1930, new and return visits to the clinic and hospital being used for comparison.

Depressions in the cumulative monthly incidence were noted for February, September and December, with the highest point in August. These variations were more marked among women with the exception of February, when the depression was also marked for men.

The proportion of cases of women to those of men was approximately 1 to 1.3.

The age of greatest incidence was from 16 to 60. Age groups of the population were used for comparison.

A tabulation of occupations and a list of the sites involved in persons engaged in each is given. It will be noted that practically no occupations other than those of city dwellers are recorded. Records of cases in other than city dwellers would be interesting.

The prevalence of involvement of the hands in women and of the feet in men is stressed. An attempt is made to explain the difference from the standpoint of foci, allergy, habits, occupation and physical build.

The chronicity of the lesions is discussed.

A contour chart of the site of involvement for the years from 1926 to 1933 inclusive is given.

Other diseases in the patient are listed when it is thought that they might be of interest.

Minor Notes

RECURRENT HERPES ZOSTER (FEMORALIS)

Report of a Case with Unusual Features

ARTHUR SAYER, M.D., NEW YORK

A case of herpes zoster usually does not excite much interest unless there is present an unusual manifestation. In the following case the patient had two attacks within five months. The first time the eruption occurred on the left leg, and the second time, on the right leg. The individual vesicular lesions were surrounded by a distinct bright red purpuric zone, and most of the vesicles were filled with a bluish hemorrhagic exudate. In spite of the hemorrhagic character, no gangrenous lesions developed, and there was no scar formation.

P. L., a white man, retired, aged 73, born in Russia, first presented himself at the dermatologic clinic of the Morrisania City Hospital on Feb. 8, 1935, on account of a painful eruption on the left leg which he stated had been present for four days. The eruption consisted of a few groups of hemorrhagic vesicles and covered an area about 6 cm. in diameter on the anterior aspect of the middle third of the left leg. He complained of pain in this leg since the onset of the eruption. The diagnosis was herpes zoster. With the use of a bland ointment locally and acetylsalicylic acid to relieve the pains, in the course of the next two months the patient made an uneventful recovery.

There were brownish-red areas of pigmentation left behind at the site of the lesions which were noticeable when he returned to the clinic on July 23. At this time he complained of an eruption on the right leg, with pains shooting down the right leg, which he stated had been present for the past six days. There were several groups of vesicles on the lateral and posterior aspects of the upper half of the right leg. Each vesicle was surrounded by a distinct bright red hemorrhagic zone. There was also a diffuse pinkish area, roughly about 15 cm. in diameter, which surrounded the entire eruption (lymphangitis). There were noted a few isolated vesicles, of similar character, near the right ankle. These aberrant lesions appeared simultaneously with the main eruption of herpes zoster.

The patient said that he had not taken any drugs by mouth and had not received any intravenous or subcutaneous injections. He had not suffered an injury to his spine at any time. He had always been in good health, and there had never been any neurologic symptoms.

Laboratory examinations were made with the following results: The Wassermann and Kahn reactions of the blood were negative. Urinalysis showed a specific gravity of 1.016, an amber color, an acid reaction, no albumin and a very faint trace of sugar. The microscopic examination of the urine gave negative results. A blood count revealed 4,980,000 red cells, 80 per cent hemoglobin, no abnormalities in the smear of the red cells, and 10,200 white cells, with 71 per cent polymorphonuclears, 22 per cent lymphocytes, 1 per cent monocytes, 3 per cent eosinophils and 3 per cent transitionals.

A RESTRAINING JACKET FOR PREVENTION OF SCRATCHING

LEON GOLDMAN, M.D., CINCINNATI

The restraining appliance to be described has been used chiefly in cases of flexural eczema. However, it may be used in almost any disease of the skin in which pruritus is disturbing. The idea was suggested by a patient. A man's coat is used, usually the coat of a suit. The sleeves are sewed down tightly to the back of the coat, with the end of the sleeves left open. The coat is then put on backward and buttoned securely in the back. As an additional precaution, boxing gloves or large cotton balls may be used to cover the hands. If the patient has any trouble at night in retaining the covers when he is in this modified straight-jacket, the ends of the covers, at the top, may be fastened to the bed with large safety pins. Patients wearing this restraining jacket have been watched throughout the night, and they are fairly comfortable. Their involuntary purposeful movements at night do not disturb the jacket. If the coat on top of the dressings is too hot at night, a lighter coat may be used.

As mentioned previously, this garment has been used chiefly in the treatment of adults with eczema. However, it can be adapted readily for use on patients with other pruritic dermatoses and on patients of other ages.

BRILLIANT GREEN FOR TREATMENT OF BLEPHARITIS

LOUIS TULIPAN, M.D., NEW YORK

A 1 per cent aqueous solution of brilliant green (tetra-ethyl-di-amino-triphenylmethane sulfate) painted on the eyelids daily for several weeks has proved efficacious in the treatment of a few patients with blepharitis associated with sycosis vulgaris. Care must be taken not to allow the solution to touch the conjunctivae. The patient can wear smoked glasses to avoid attracting undesired attention.

Correspondence

RÔLE OF IODINE IN THE THERAPY OF SYPHILIS

To The Editor.—The article by E. T. Burke on the "Rôle of Iodine in the Therapy of Syphilis," which appeared in the September issue of the ARCHIVES (**32**:404, 1935), is of considerable interest to me since its entire subject matter revolves about an article written by Cobane and myself entitled "Syphilitic Fibrosis and the Status of the Iodides in the Present-Day Treatment of Syphilis," which appeared in the *American Journal of Syphilis and Neurology* in July 1934 (vol. 18, p. 289).

In his article Burke briefly reviews the pathology of syphilis, the mechanism of the destruction by the body ferments of Spirochaeta pallida, the action of the iodides as based on the work of Jobling and Petersen and on the work of Giemsa and Levaditi in connection with the production of a protein bismuth compound termed "bismoxyl" by Levaditi—the spirocheticidal substance formed after bismuth is injected into the tissues. If, in connection with this last observation, it is Colonel Burke's idea that bismoxyl, which is but spirocheticidal, cannot therefore dissolve fibrous tissue (I presume he means syphilitic fibrous tissue), it might be said in refutation that fibrous tissue is never avascular as Burke stated, although the size and number of blood vessels may be greatly reduced; that bismoxyl may enter through the few blood vessels such tissue still possesses, destroy the organisms it supposedly encapsulates and by removing the irritant, that is S. pallida, thus remove the necessity for the overproduction of such fibrous tissue. The excessive fibrous tissue is then theoretically removed by the ferments presumably existing in the lymphoplasmacytes.

The principal object, however, of his entire review is to point out the effects and presumably the value of the iodides in cases of syphilis. Let me say at once that nowhere in our article do we deny that the iodides heal syphilitic lesions, although modern thought is almost unanimous in believing that these drugs have little or no effect on syphilis per se. The well known dissolving effect on syphilitic lesions possessed by the iodides needs no emphasis, and we agree with that part of Colonel Burke's article which indicates this and the mechanism by which it is accomplished. The iodides, however, are nonspecific agents, and irrespective of what they do to visible lesions of syphilis or the mechanism of their action, they act, in a broad sense, in no wise differently in syphilitic lesions than do other nonspecific agents. Wright and I, several years ago, demonstrated the ease with which one could cause complete resolution and disappearance of secondary and tertiary lesions (gummas and gummatous infiltrations and undoubtedly similar invisible visceral lesions) by means of intramuscular injections of a 4 per cent suspension of milk protein. It has been demonstrated that numerous other agents (nucleinates, bacterial suspensions, sulfur in oil, malaria and fever-producers of whatever nature) will do exactly the same thing. I have observed patients with syphilis of the central nervous system with accompanying tertiary lesions of the skin in whom the cutaneous lesions cleared up entirely during induced malarial paroxysms only to reappear again shortly after the patient had recovered from the induced malaria. These patients were permitted to have from sixteen to twenty febrile paroxysms. This observation indicates, of course, that nonspecific agents, even one as powerful as malaria, fail to destroy all, if

they destroy any, of the organisms present, but the point I wish to make is that these agents have a dissolving effect on organized and unorganized syphilitic exudates.

Burke speaks of the administration of the iodides with prophylactic purposes in view, the idea being to prevent the formation of the fibrosis which usually accompanies chronic syphilis. If this manner of view is correct it seems to me that unless such a nonspecific agent is administered regularly and continuously during the entire duration of the patient's disease (i. e., life), it will fail in its object. Iodides, it must be remembered, are eliminated fairly rapidly. In connection with this question of prophylaxis, it is of interest to note that persons who contract malaria before the onset or during the course of syphilis are in no way, as has been observed, guaranteed against the development of dementia paralytica at some future date.

In connection with our article, we stated that no clinical form of syphilis can lend itself to the study of the fibrolytic or fibrous tissue-dissolving effects of the new antisyphilitic remedies as does fibroid gumma (subcutaneous fibroid syphiloma) —an uncommon but well defined fibrosing type of tertiary syphilis. The histologic structure of these lesions has been carefully studied, and we have corroborated such previous histologic studies. The lesions show very definite partly and completely formed new connective tissue—so much that a competent pathologist, after examining a section from one of them, returned his report with the diagnosis of simple fibroma. Under antisyphilitic therapy (arsphenamines and bismuth), in previously reported cases and in our own as well, there was in some complete, and in others almost complete, regression of the fibrotic lesions. This, in our opinion, bespoke a special quality of some of the fibrotic tissue produced in syphilis—a quality which permits fibrolytic action in some of the fibrous tissue present in cases of chronic syphilis but not at all obtainable in the final replacement fibroses such as one sees in the skin and mucous membrane (after the serpiginous or ulceronodular syphilid), in the cornea (following prolonged keratitis) and presumably within the body.

Throughout this discussion I shall use the term syphilitic fibrous tissue to indicate this special fibrous tissue and to distinguish it from replacement fibroses which are no longer syphilitic.

The conclusions in our study were based on such clearcut evidence that there can be but one logical explanation for the complete or almost complete resolution of the fibrous tissue present in the fibroid gummas under our observation and under the observation of others before us, namely, that they not only perform on syphilitic fibrous tissue what the iodides perform but have, as is known, the added quality of destroying S. pallida. The expression "dissolving the fibrous tissue with iodides in order that the encapsulated organisms may be reached" is in reality an expression which originated in the days before arsphenamine and bismuth therapy and undoubtedly developed as a result of the inactivity of mercury in a good many cases. The reason for this inactivity of mercury has only recently been determined by the studies of Sollmann and his co-workers (ARCH. DERMAT. & SYPH. **32**:1 [July] 1935.

Most therapeutists when using iodides do so not in cases of acute but in cases of chronic syphilis with the idea of dissolving fibrous tissue, not of course replacement fibroses (which cannot be influenced by any therapy), but organized syphilitic fibrous tissue. (The fibrous tissue we saw in our histologic study differed in no way so far as visual appearance was concerned from the fibrous tissue seen in fibromas, keloids and syphilitic scars.) Such tissue must be present in cases of chronic syphilis in addition to clearcut scars—the first

influenced but the latter uninfluenced by drugs or any other agents and the iodides in particular. We felt that there must be a special quality to a fibroid tissue which is capable of undergoing resolution but which quality is completely lost when it takes the form of a scar or replacement fibrosis.

We presented a photomicrograph of a section of one of the fibrotic nodules removed from the forearm of a patient with juxta-articular nodules. It portrays the large amount of fibrous tissue present in such nodules as well as the variously sized perivascular collections of round cells usual to syphilitic tissue. This was ideal material to demonstrate the dissolving effects of the organic arsenicals and the bismuth preparations. It was evident from the action of these drugs in this fibrous tissue that what Colonel Burke states the iodides will do for granulomatous and fibroid tissue the new antisyphilitic drugs will likewise do. This means in the first place that there is no necessity for fibrolytic agents as represented by the iodides, first, to prevent replacement fibroses and, second, to enable spirocheticidal drugs to reach the organism if it can be shown (as it indeed was) that these spirocheticidal drugs do exactly what the iodides do, and especially since they are at the same time spirocheticidal. If the arsphenamines and bismuth preparations do this to visibly organized syphilitic fibrous tissue, is there any reason to believe that the invisible lesions of similar nature within the body are not influenced in exactly the same way?

We note with astonishment Colonel Burke's first conclusion, to wit: "Iodide plays a valuable rôle in the treatment of syphilis in every stage." This is certainly contrary to modern American thought on antisyphilitic therapy, certainly in respect to early syphilis, as evidenced by the treatment schedules prepared by Wise and Sultzberger in "The Year Book of Dermatology and Syphilology" (Chicago, The Year Book Publishing Co., 1934, pp. 8, 14 and 15) by the treatment systems given by Stokes in his textbook, "Modern Clinical Syphilology" (Philadelphia, W. B. Saunders Company, 1934, pp. 552 and 553) and the suggested standard treatment resulting from the cooperative clinical studies sponsored by the United States Public Health Service, published in *Venereal Disease Information* (**15**:153 [April] 1934). All of these charts are concerned with the treatment of seronegative and seropositive primary and secondary syphilis—that is, with early syphilis. In none of these are the iodides mentioned as part of the treatment.

No one ever thinks in terms of fibrosis when considering early syphilis—that is why one treats the disease syphilis in this stage and the patient rather than the disease in the later stages of syphilis. It is only fair to state that in a chart outlining a scheme of treatment for early syphilis, in the same issue of *Venereal Disease Information*, there is advised one month's treatment with iodides, from the eighth to the twelfth week of treatment for acute syphilis, i. e., one month of administration of iodides when treatment is advised over a period of one hundred and twenty-three weeks.

It is true that my definition for acute syphilis (*Therap. Gaz.* **51**:1 [Jan. 15] 1927) is somewhat more elastic than is the definition given by Colonel Burke, but when one considers that lesions in no way different clinically from those of the secondary stage have been seen as late as eight years after the initial lesion (I have seen commissural secondary papules four years after the initial lesion), but such relapsing ones commonly from one to two years after the primary lesion, the long arbitrary period given by us for acute syphilis is not so serious and fits in with the facts.

So far as chronic syphilis is concerned, it is generally admitted that the iodides are exhibited purely for their fibrolytic activity. We feel that we have shown that the new drugs are definitely fibrolytic in the presence of syphilitic exudates which have undergone partial or complete fibrosis.

Colonel Burke states: "From the very beginning of the syphilitic infection there is a tendency for the essential lymphocyte and plasma cell reaction to progress in the direction of fibrosis. . . . It is but prudent, then, and in accordance with the dictates of common sense, to neutralize from the earliest moment the power of the lipoids by saturating them with iodine."

Inasmuch as the arsphenamines and the bismuth preparations accomplish the same purpose, why give the iodides at all? We ask this question especially as Burke further states: "One serious drawback to the oral method of giving iodine is that outpatients may not take the drug regularly, if at all. Sodium iodide may be given intravenously, but reaction is apt to occur, and the method cannot be recommended as routine procedure."

With the arsphenamines and with the bismuth preparations, however, the patients are given their medicine in such a way that they carry it with them (intravenously or intramuscularly).

Burke states: "There is no evidence to support the suggestion that arsphenamine and bismuth can deputize for iodine and the iodides. They are used for different purposes." We reiterate our belief that they may be used for the same purposes—to dissolve syphilitic fibrogenic tissue and in addition to destroy S. pallida. The shortcomings of modern antisyphilitic therapy lie not in the fact that the iodides are being used to a lesser extent but in the many factors connected with modern drugs and the patients, as a study of the literature on resistant syphilis clearly indicates. Finally, Burke states: "Short of complete scarring, the denser the fibrous tissue the more need there is for the iodides to open the way for the assault by the spirocheticidal drugs." It is difficult to understand what he means by this, as there is no pathologic difference between complete scarring and his so-called denser fibrous tissue, but, as I have pointed out, there is a clinical difference and an inherent difference which can be determined by both nonspecific and specific antisyphilitic agents.

On page 410 Burke speaks of the "therapeutic paradox" and paints a horrible picture of what would happen to a patient with syphilitic hepatic cirrhosis if he were given arsphenamine or bismuth. It has been given to few physicians, no matter how extensive their practice in handling patients with syphilis, to see "the liver reduced to an inert mass of fibrous tissue" by such medication. Let me call Colonel Burke's attention to the fact that Udo Wile (not Stokes), as quoted by Moore in his recent textbook on the "The Modern Treatment of Syphilis" (Springfield, Ill., Charles C. Thomas, Publisher, 1934, p. 285), drew attention to this phenomenon several years ago. He pointed out that in certain patients with cardiovascular syphilis and with previously adequate cardiac compensation treatment resulted in an initial period of symptomatic improvement which was followed by the sudden appearance of congestive heart failure, probably due to too rapid healing of the syphilitic inflammatory tissue now replaced by a scar greatly interfering with the function of that organ. Wile applied the same reasoning to the syphilitic liver, but in our clinic, as in the clinic of Moore (Moore's textbook, p. 304), the therapeutic paradox, so far as hepatic disease is concerned, has been of little importance. Even if the therapeutic paradox were to be feared as much as Colonel Burke believes it should be, there still is no valid reason against using weaker or smaller doses of the stronger bismuth compounds to prevent such a complication.

Burke believes that our term "fibrolytic" in the quotation from our article "fibrolytic in the presence of syphilitic fibrogenic exudates" was unwarrantable. I might say that throughout our article the term was, with this one exception, placed in quotation marks to call attention to the fact that such action depended on a special quality of the fibrous tissue which certain syphilitic fibrous tissue has. Burke states on page 410: "It is granted that when the fibrosis is not too dense and avascular . . . the lesion will . . . become smaller and will eventually be converted into scar tissue. But this is not due to any truly fibrolytic effect of these preparations on the tissue. . . . There is no true absorption of the fibrogenic material but only a conversion into ordinary normal scar tissue."

Whether the disappearance of the fibroid tissue or the fibrolysis takes place directly or only after the irritant (the organism) has been destroyed makes little difference. The agent causing it is still a fibrolytic one and the process still fibrolytic. In our article we desired to make the point that this process took place in the presence of syphilitic fibrogenic exudates (not all syphilitic exudates are fibrogenic—witness the spontaneous and complete scarless disappearance of most cutaneous and oral primary and secondary syphilids). As to the statement that Burke makes that fibrogenic material is not absorbed but is converted into scar tissue, this is refuted by our studies and by the fact that there are few who have not seen oral and cutaneous gummas disappear without the vestige of a sign indicating their former location.

Burke further states: "In chronic syphilis it must be remembered that in addition to gummas which are clinically evident there are present in important visceral organs gummatous infiltrations which have not yet given rise to any symptom. In every instance of chronic syphilis—in males at least—such lesions are present in the aorta. While it is true that arsphenamine and bismuth will kill the spirochetes which cause these lesions and thus bring about their regression and repair by fibrous scar tissue, the resultant scar is protective. In such cases the administration of iodides may cause too great an absorption and so weaken the wall of the vessel."

This paragraph is slightly ambiguous. Take for example the sentence after "resultant scar is protective," if iodine cannot dissolve visible, definite, post-syphilitic scar tissue (such as is seen after oral or cutaneous tertiary lesions), just how can it dissolve similar tissue within the body? How could it possibly cause absorption and resultant weakening of the wall of the aorta? Such a calamity can occur only, as it occasionally does, in connection with an aneurysm, in which case rupture may result from the too rapid absorption of the syphilitic fibrous tissue—so rapidly that as the protective syphilitic fibrosis resolves the naturally forming protective scar tissue gets no chance to catch up and protect that wall from the normal pressure from within. Why would not an iodide be administered in such a case? It is the drug (although we prefer bismuth) indicated since it dissolves syphilitic fibrous tissue slowly, which is exactly what such a situation demands, namely, time for the development of the natural protective scar.

Burke continues: "In considering any case of chronic syphilis it is necessary to decide whether or not the fibrosis which is present is preponderantly protective, and, when it is, the only safe rule is to withhold iodine. In such patients, when arsphenamine and bismuth only are used it seems that the resolution of these lesions proceeds more slowly and that the repair tissue is thicker and more resistant than when iodine therapy has been adopted."

It is indeed a problem to determine whether or not the fibrosis present in any case of chronic syphilis is, as Colonel Burke states, "preponderantly protective."

I am at a loss to understand by what legerdemain such a state of affairs is to be diagnosed. Finally, Colonel Burke speaks of the "thicker and more resistant repair tissue" produced by the arsphenamines and bismuth. I do not know in the first place on what basis such a statement is made and in the second place to what drug the tissue would be more resistant; finally, if this really was the fact and arsphenamine and bismuth produced scars of the type described, they would be ideal for such areas as the walls of blood vessels and the aorta in particular and clearly they, rather than the iodides, would be the drugs indicated.

SIGMUND S. GREENBAUM, M.D., Philadelphia.

USE OF AUTOGENOUS FUNGUS EXTRACTS IN THE TREATMENT OF MYCOTIC INFECTIONS

To the Editor:—In the issue of the ARCHIVES of November 1935 (vol. 32, p. 787) is an article by Robinson and Grauer, entitled "Use of Autogenous Fungus Extracts in the Treatment of Mycotic Infections." In their concluding remarks these authors stated: "A series of patients with mycotic infections successfully treated with autogenous extracts is reported." Also: "Clinical and bacteriologic cures obtained by treatment with fungus vaccine recommend it as a means of therapy for refractory dermatomycoses."

These statements indicating good results are much at variance with those made in other articles, notably those of Traub and Tolmach (Dermatophytosis: Its Treatment with Trichophytin, ARCH. DERMAT. & SYPH. **32**:413, [Sept.] 1935. Transactions of the Ninth International Congress of Dermatology, Budapest, Hungary, Sept. 13 to 21, 1935, p. 714). Traub and Tolmach stated: "It seems to us that in evaluating a remedy for such a capricious disease as superficial dermatophytosis with or without 'ids', credit should be given only for cure or marked improvement. Using such a criterion, we fail to see any rational basis for considering that intradermal injections of trichophytin are particularly useful in the treatment of this disease."

The use of fungus extracts for therapeutic purposes dates back to 1908. Since that time many clinicians have investigated this form of therapy. Among others, Takahashi employed it in superficial fungus infections before 1924. (Use of Trichophytin in Trichophytia, with Especial Reference to Superficial Varieties, *Jap. J. Dermat. & Urol.* **24**:83, 1924). Three years ago Sulzberger and I directed attention to the procedure in several publications and discussions (Ringworm and Trichophytin: Newer Developments, Including Practical and Theoretical Considerations, *J. A. M. A.* **99**:1759 [Nov. 19] 1932). The therapeutic effects obtained by us were not as promising as was anticipated, but the investigators held out hopes for better results, commensurate with improvements in the preparation of the extracts, better technic, better controls, more extensive clinical material, etc.

Last year Templeton advocated the employment of greatly diluted extracts (Krueger and Templeton: Preparation of Trichophytin, ARCH. DERMAT. & SYPH. **30**:9 [July] 1934). Several colleagues have informed me that the greatly diluted extracts appear to be of distinct value, as compared with the dilutions previously recommended and used. In connection with this problem, mention should be made of a Brazilian product, manufactured in the laboratory of de Fonseca in Rio de Janeiro, Brazil; it is highly recommended by Brazilian dermatologists for the treatment of fungous infections and is available in this country.

It appears desirable to have a large group of dermatologists investigate the effects of the intradermal use of fungus extracts and to "pool" their findings on the great numbers of patients undergoing treatment in the United States and Canada (as is being done in co-operative investigations on syphilis by groups of American dermatosyphilologists). Such work is being conducted at present in the mycology department of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, in my service.

By "pooling" the findings on many patients, employing suitable controls and improved methods, dermatologists could clarify a nebulous terrain and conserve much work and time.

FRED WISE, M.D., New York.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

ERUPTIVE FEVER WITH STOMATITIS AND OPHTHALMIA: ATYPICAL ERYTHEMA EXUDATIVUM MULTIFORME (STEVENS-JOHNSON). GEORGE J. GINANDES, Am. J. Dis. Child. **49**:1148 (May) 1935.

Ginandes reports a case of an eruption with associated cutaneous, buccal and ocular lesions. In the syndrome under consideration the cutaneous lesions are generalized brownish-red to dark red maculopapules, in some of which yellow dry necrotic centers developed later. The onset is sudden, and the constitutional symptoms include malaise, extreme restlessness and burning sensations associated with a temperature of from 101 to 104 F. The buccal mucosa is inflamed and eroded, and bullae may be present.

Purulent conjunctivitis with marked edema of the eyelids is a constant finding, and the ocular symptoms and sequelae are uniformly severe, generally resulting in corneal opacities and partial or complete blindness. There is either a leukopenia or a mild leukocytosis.

After reviewing reports of similar cases in the literature Ginandes states that the condition is either a distinct clinical entity or an atypical form of erythema multiforme.

ALLERGIC ECZEMA: ECZEMA INITIATED BY SENSITIZATION OF FOODS. J. G. HOPKINS and B. M. KESTON, Am. J. Dis. Child. **49**:1511 (June) 1935.

Since the publication in 1930 of their study of specific sensitivity in cases of eczema, Hopkins and Keston have studied a larger series of cases and have again found that in the majority of infants allergy to food was the sole cause of the eruption and that even in a number of older patients this factor was important. In seventy-five of four hundred cases there was definite evidence that food was either the sole cause (60 per cent) or a contributing cause (36 per cent) of the dermatosis. The foods found to be the cause of the eruption, as listed in order of frequency, were: eggs, wheat, milk, orange, spinach, oat, cod and potato. Artificial desensitization by mouth was successful in many cases. The use of propeptan tablets produced disappointing results.

In ascertaining the offending foods Hopkins and Keston found that cutaneous tests were not decisive without confirming dietary tests. Foods which caused a definite positive reaction usually seemed to aggravate the eruption, but a negative reaction was no indication that the corresponding food was not concerned with the patient's eczema. Elimination diets such as those devised by Rowe were found to be the most useful method for the clinical determination of sensitivity to food.

COMPARATIVE VALUES OF CUTANEOUS, PERCUTANEOUS AND INTRACUTANEOUS TUBERCULIN TESTS IN CHILDREN. SPECIAL REFERENCE TO SENSITIVENESS OF THE PLASTER TEST. G. ANZÉN, Am. J. Dis. Child. **50**:104 (July) 1935.

Anzén attempted to determine the reliability of the tuberculin plaster test. Of 2,183 patients 307 showed positive reactions to both the plaster and the Pirquet test and 1,838 showed negative reactions to both tests. Thus the results of the two tests were in agreement in 98 per cent of the cases. In 10 cases the Pirquet test gave a negative reaction while the reaction to the plaster test was positive; in all these 10 cases there was a positive reaction to the Mantoux test. Of the 1,838 patients who showed a negative reaction to both the plaster and the Pirquet

tests, 806 were further tested by Mantoux's method. Only 11 (1.25 per cent) reacted positively. Anzén believes that in febrile states the plaster test is much more sensitive than the Pirquet test and that if the plaster test were the only means employed only 1.25 per cent of the positive reactions would fail to be detected.

ELIMINATION DIETS FOR CHILDREN. CLEMENT B. P. COBB, Am. J. Dis. Child. **50**:187 (July) 1935.

After discussing the general indications for elimination diets in children Cobb outlines points to be considered in the selection of an appropriate trial diet. Seven type diets for children are then presented in detail, and recipes are given. These seven diets may be roughly classified as follows: Diets 1 and 2, without milk, egg and wheat; diet 3, without egg and wheat, with milk; diet 4, without egg and milk, with wheat; diet 5, without milk; diet 6, without wheat; diet 7, without egg.

NELSON PAUL ANDERSON, Los Angeles.

GLAUCOMA ACCOMPANYING NAEVUS FLAMMEUS. EDWIN B. DUNPHY, Am. J. Ophth. **18**:709 (Aug.) 1935.

To the sixty-one recorded cases of glaucoma associated with naevus flammeus Dunphy adds two new cases. In one of these in which histologic examination was made, as well as in nine of the thirteen reported cases in which a similar examination was made, there were angiomatous changes in the uvea as well as dilatation of the intra-ocular capillaries. Dunphy advances the theory that in these cases the glaucoma is attributable to obstruction of the filtration angle due to angiomatous changes in the uvea or to adhesions in the iris resulting from degenerative changes.

WIEDER, Milwaukee.

ON THE INCIDENCE OF SYPHILIS IN THE AMERICAN NEGRO. R. S. JASON, Am. J. Syph. & Neurol. **19**:313 (July) 1935.

A study of the Wassermann tests made on 4,595 Negro patients at the Freedmen's Hospital from Jan. 1 to Dec. 31, 1933, revealed 19.41 per cent positive reactions.

The age, sex, hospital service, address, place of birth and particularly the socio-economic level, as indicated by the occupations of the patients studied and the persons with whom they lived, were associated with significant variations in the incidence of syphilis. Marital status did not materially affect the incidence of syphilis as revealed by this study.

ARSPHENAMINE POISONING OCCURRING AMONG NEGRO WOMEN. G. WALSH and C. S. STICKLEY, Am. J. Syph. & Neurol. **19**:323 (July) 1935.

Walsh and Stickley are of the opinion that occurrence of arsphenamine poisoning is more common than is generally supposed, and they report eleven cases occurring in Negresses.

The mental attitude of Negroes, marked by disinterestedness, secretiveness and a certain callousness toward their own suffering, and the fact that the symptoms and cutaneous changes in Negroes do not receive the attention that they do in Caucasians are believed to be the chief reasons that these cases are not discovered in time to prevent severe symptoms and, occasionally, death. The fragility and small caliber of the veins of Negresses and the difficulties incident to giving the arsphenamine without spilling into the perivenous tissue are suggested as reasons for the frequency of arsphenamine poisoning in Negresses. Walsh and Stickley are enthusiastic regarding the value of epinephrine in allaying the itching in cases of dermatitis due to arsphenamine.

SYPHILITIC ANEMIA WITH DIFFUSE OSTEITIS AND SUPERINFECTION. E. B. TAUBER and L. GOLDMAN, Am. J. Syph. & Neurol. **19**:339 (July) 1935.

Tauber and Goldman report the case of a Negro with a severe macrocytic anemia, extensive gummatous osteitis of the bones, meningitis and a probable superinfection of the glans penis, all apparently various manifestations of syphilis. The patient also had symptoms resembling those of Darier's disease. The authors are of the opinion that severe anemia, resembling pernicious anemia, can and does occur in patients with syphilis and responds to antisyphilitic treatment.

REUTER, Milwaukee.

HICCUP CRISIS IN TABES DORSALIS. CHARLES METCALFE BYRNES, Bull. Johns Hopkins Hosp. **56**:264 (May) 1935.

Byrnes reports a case of persistent hiccups which occurred in a tabetic patient six hours after the subdural administration of mercurialized serum containing 1/50 grain (0.0013 Gm.) of mercuric chloride. The hiccups persisted for nine days in spite of many various therapeutic measures including spinal puncture and chloroform anesthesia. The hiccups were finally controlled by the subdural injection of mercurialized serum.

The author cites a similar case and gives a review of the literature.

THE TREATMENT OF INTRACRANIAL HEMORRHAGE RESULTING FROM CISTERNAL PUNCTURE. WALTER E. DANDY, Bull. Johns Hopkins Hosp. **56**:294 (May) 1935.

Dandy reports a case of intracranial hemorrhage following a cisternal puncture. He points out that this accident resulted from anatomic factors which were unusual but not uncommon. In this instance, as in many cases, the cerebellar tonsils projected into the foramen magnum and greatly reduced the size of the cisterna magna. Indeed after an extensive operative experience in that field Dandy wonders why such accidents do not happen more frequently. He mentions a fatality that occurred in his own practice, a tumor having pushed the medulla tightly against the dura and obliterated the part of the cisterna magna lying between these structures.

SYPHILITIC MYOCARDITIS. THOMAS P. MAGILL, Bull. Johns Hopkins Hosp. **57**:22 (July) 1935.

Magill lists a group of twenty cases of cardiac disease in which there was decompensation but no evidence of any organic valvular disease. In no case was there any definite history of rheumatic fever, chorea or scarlet fever, and hypertension, nephritis or anginal attacks were not present. All the patients in the group had positive Wassermann reactions or had previously received antisyphilitic treatment. Eighteen of the patients were Negroes. Five of the patients were examined post mortem, and the only pathologic changes in the hearts were the extensive scarring of the cardiac muscle and infiltration of the myocardium, endocardium and epicardium with round cells. None of these patients showed typical syphilis of the aorta. Magill's observations in these cases and in cases of definite syphilis of the aorta and aortic valve suggest that if this scarring and round cell infiltration is of syphilitic origin the condition may occur quite independently of syphilis of the aorta. In conclusion he expresses the belief that these cases represent instances of syphilitic myocarditis.

NELSON PAUL ANDERSON, Los Angeles.

LATENT SYPHILIS. S. C. PETERSON, Canad. M. A. J. **32**:655 (June) 1935.

In 50 per cent of a group of untreated syphilitic patients some type of lesion developed in a late stage of the disease, 50 per cent of the lesions being wholly

incapacitating or fatal. There was only a 16 per cent chance that an untreated syphilitic woman would have a living healthy child as compared to a 76 per cent chance in the average nonsyphilitic woman. For these and for other reasons latent syphilis should always be treated except in aged patients or when it is associated with some serious concurrent malady.

ECZEMA. H. ORR, Canad. M. A. J. **33**:173 (Aug.) 1935.

The subject was reviewed from the etiologic standpoint. The multiplicity of causes made the treatment dependent on an exact diagnosis.

MADUROMYCOSIS; WITH THE REPORT OF A CASE DUE TO MONOSPORIUM APIOSPERMUM. R. M. SHAW and J. W. MACGREGOR, Canad. M. A. J. **33**:23 (July) 1935.

Shaw and Macgregor report the first case of maduromycosis from Canada. The infection apparently originated in Kansas. Amputation was necessary.

MONOSPORIUM APIOSPERMUM, A FUNGUS CAUSING MADURA FOOT IN CANADA. E. S. Dowding, Canad. M. A. J. **33**:28 (July) 1935.

Dowding reports the result of a mycologic study of a fungus isolated from the lesions of a patient with maduromycosis.

THE COMPARATIVE TENDENCY OF KRAUROSIS AND LEUKOPLAKIA OF THE VULVA TO BECOME MALIGNANT. P. J. KEARNS, Canad. M. A. J. **33**:48 (July) 1935.

Care should be exercised in distinguishing between diseases of the vulva such as vulvitis, syphilis, kraurosis vulvae, leukoplakia and cancer. Kearns found that the incidence of cancer was much greater after leukoplakia (from 20 to 25 per cent) than after kraurosis or inflammatory conditions.

A RAPID TEST FOR SYPHILIS. G. F. LAUGHLEN, Canad. M. A. J. **33**:179 (Aug.) 1935.

According to Laughlen the advantages of a new agglutination method for the detection of syphilis are that the method is rapid and inexpensive and that the test is easily performed without special training. There was 98 per cent agreement between the reaction to the new test and the Wassermann reaction and 99 per cent agreement with the Kahn reaction. The method is proposed as adaptable for routine use in smaller hospitals and clinics as well as for emergencies in larger hospitals.

LEWIS, New York.

LEUKOPLAKIA BUCCALIS AND CANCER. SOMERS H. STURGIS and CHARLES C. LUND, New England J. Med. **212**:7 (Jan. 3) 1935.

Detailed studies were made in 248 selected cases of leukoplakia and keratosis of the mouth or lip which were observed over a period of five years, with special scrutiny of etiologic factors. In twenty-five cases carcinoma developed while the patients were under observation, and twelve of these patients died. The usually indicted elements of age, sex, syphilis, use of tobacco and poor dental hygiene were found to be of far less importance than those of delay in reporting for care, extent of the lesion, inadequate treatment and error in diagnosis. Thus the former group of factors is of no value in predicting the likelihood of the formation of carcinoma, while the latter group is the determining agent in the outcome. Duration was not of significance, but location of the disorder in the oral mucosa led to a higher incidence of malignant degeneration than that confined to the lips.

Iodo-Bismuthate of Quinine in the Treatment of Syphilis. E. Lawrence Oliver and G. Marshall Crawford, New England J. Med. **212**:297 (Feb. 14) 1935.

Two parallel series, each consisting of seventy-six cases of uncomplicated syphilis, were compared with regard to results obtained with the use of bismuth subsalicylate and quinine bismuth iodide, especially concerning serologic reactions, albumin in the urine, dermatitis, a bismuth line, stomatitis, etc. The results suggest that the quinine bismuth iodide, in spite of its lower bismuth content, is superior to bismuth subsalicylate. The complications occurring during treatment were also studied in 118 other cases in which both preparations had been used, and a similar conclusion was reached because of the smaller number of unfortunate accidents occurring in the patients receiving quinine bismuth iodide.

Lymphomogranuloma Inguinale. Marion E. Howard and Maurice J. Strauss, New England J. Med. **212**:323 (Feb. 21) 1935.

Sixteen cases of lymphogranuloma inguinale found in and around New Haven, Conn., are reported in detail. Eleven were in male patients, of whom eight were white and three were Negro. The five women were all Negresses and had rectal strictures. The Frei antigen elicited a positive cutaneous reaction in all cases. Typical inguinal adenitis was observed in ten men, two of whom had early general systemic reactions.

A Clinical Evaluation of the Positive Skin Reaction in Asthma, Urticaria, Vasomotor Rhinitis and Seasonal Hay Fever. Abraham Colmes, New England J. Med. **212**:725 (April 18) 1935.

The records of 250 patients with asthma, 93 patients with urticaria, 222 patients with perennial vasomotor rhinitis and 314 patients with seasonal hay fever were reviewed, and the relationship of the positive reactions to the patients' symptoms was noted. In the patients with asthma, 40 per cent of the reacting proteins were of diagnostic importance; 4 per cent of the patients with urticaria, 25 per cent of those with perennial vasomotor rhinitis and nearly 100 per cent of those with seasonal hay fever reacted to the pollens which were causative of their disease. These results indicate that in the study of allergic diseases the positive cutaneous reaction cannot be accepted as a sole basis for determining the offending factor but that a careful consideration of the clinical history may be of as much value. This again shows that a laboratory test should not displace entirely a detailed clinical consideration of the patient. It seems that promiscuous testing of the skin should become a thing of the past. Proper selection of patient and of test should be made in order to gain the proper scientific data and to avoid subjecting the patient to unnecessary tests and expense. At the same time thought should be given to the variation in tests from time to time. Their evaluation demands experience and common sense. Further studies will undoubtedly clarify the situation still further and stabilize the value of the tests in their proper diagnostic niche.

Surgical Problems of Fungous Origin: Report of a Case of Sporotrichosis in Massachusetts. John G. Downing, New England J. Med. **212**:1085 (June 6) 1935.

Downing reports a case of sporotrichosis occurring in a boy; the infection followed an abrasion of the right index finger on a nail in the cellar of the patient's home. Swelling and redness of the metacarpophalangeal joint appeared and persisted under local application of heat. Two months later red, tender, hard lumps appeared on the medial aspect of the forearm and arm. Repeated incision and drainage were of no avail. When the patient was admitted to the dermatologic service of the Boston City Hospital sporotrichosis was suspected, and its presence was proved by the positive results of a culture of Sporotrichum Schenckii. The white blood cell count was 19,600. A slight cough developed, and the patient lost 14

pounds (6.4 Kg.), but no pulmonary lesion was demonstrated. The condition responded to local application of 1 per cent solution of tincture of iodine and administration of increasing doses of potassium iodide. The course was afebrile. A brief discussion of the surgical complications of fungous infection is appended, and emphasis is laid on the possibility of epidermomycosis as the portal for secondary infection leading to serious surgical conditions.

A Study of Heart Disease Among Veterans: Syphilitic Heart Disease. Philip B. Matz, New England J. Med. **212**:1087 (June 6) 1935.

Forty-one, or 9.5 per cent, of a group of 433 patients with cardiac disease showed the presence of syphilitic aortitis. Of this number, 28 were white patients, an incidence of 7.1 per cent, and 13 were Negroes, an incidence of 12 per cent. A study of the serologic findings in the group of patients with syphilitic aortitis showed that 75.6 per cent had a positive Wassermann reaction. Of the 41 patients with syphilitic aortitis, 28, or 68.3 per cent, showed the presence of dilatation and 13, or 31.7 per cent, were free from dilatation. The average age at the time of inception of syphilitic aortitis was 33.6 years; the youngest patient was 28 and the oldest was 63 years of age. Among 18 patients with syphilitic aortitis the average duration of life from the date of inception to the date of this study was eight and six-tenths years; among 11 deceased patients the average duration of life after the onset of the disease was five and two-tenths years. The most frequent clinical symptoms and signs of syphilitic aortitis were dyspnea, palpitation, precordial pain, fatigue and cough. The most frequent coexisting anatomic cardiac conditions in patients with syphilitic aortitis were aortic insufficiency, enlargement of the heart, mitral insufficiency, chronic myocardial disease and cardiac hypertrophy. The most frequent abnormal physiologic cardiac conditions coexisting with syphilitic aortitis were aortic incompetency, hypertension, mitral incompetency and congestive cardiac failure. In the group of 433 patients it was found that 71 gave evidence of aortic insufficiency; of the latter 46 had syphilitic aortic insufficiency. Of these 46 patients 30 had coexisting syphilitic aortitis. Of the 46 patients with syphilitic aortic insufficiency, 27 were white persons, an incidence of 60 per cent, and 19 were Negroes, an incidence of 40 per cent. Eighty per cent of the patients with syphilitic aortic insufficiency had a positive serologic reaction. Of the group of 46 patients with syphilitic aortic insufficiency it was found that 24 had no coexisting cardiac valvular lesions and that 16 had a combination of aortic insufficiency and mitral insufficiency. The average age at the time of the inception of syphilitic aortic insufficiency was 24 years. The average duration of aortic insufficiency in the living patients was seven and seven-tenths years; in the deceased patients it was five and two-tenths years. Among the patients with syphilitic cardiac disease 5 gave evidence of syphilitic aneurysm of the aorta; in 3 the aneurysm was in the ascending aorta; in 1 it was in the ascending and transverse portions of the aorta, and in 1 it was in the ascending, transverse and descending portions of the aorta.

The Treatment of Acne Vulgaris with Pregnancy Urine Extract. Charles H. Lawrence and Jacob Feigenbaum, New England J. Med. **212**:1213 (June 27) 1935.

Fifteen cases of acne are reported in which treatment with a purified form of the anterior pituitary-like hormone from the urine of pregnant women has given results satisfactory enough to warrant further study. A chart is appended showing details of these cases. The authors suggest that the cause of the disorder lies in an endocrine imbalance coincident with adolescence, consisting possibly in a quantitative or qualitative abnormality of the newly activated gonadal hormones.

Sensitivity to Environmental Allergens in Infantile Eczema. Lewis Webb Hill, New England J. Med. **213**:135 (July 25) 1935.

Scratch tests for sensitivity to environmental allergens in infants with eczema were positive in 10 per cent of thirty-eight children under 1 year of age; in 37 per

cent of fourteen children between 1 and 2 years of age and in 50 per cent of forty-nine children between 2 and 12 years of age. In a series of twenty-five patients tested by means of the patch test with protein environmental allergens there were no positive reactions. Twenty-one patients who had positive reactions to scratch tests with an environmental allergen were tested by means of the patch test with the same allergen. There was only one positive reaction. This was manifested by the formation of wheals and not by the usual vesiculation and scaling ordinarily seen in positive patch tests with nonprotein substances. Of twenty-two patients who had a positive reaction to scratch tests application of the reacting protein to the unbroken skin caused an immediate formation of a wheal in only three, but when the skin was gently abraded with the end of an applicator before being brought in contact with the protein, a reaction invariably followed. (Seven patients were tested in that way.) Twenty patients were tested with ten common environmental nonprotein substances by means of the patch test. There were positive reactions in only one patient.

Hill draws the following conclusions: The substances from the epidermis of animals and other so-called environmental allergens, as well as foods, should be taken into consideration in any attempt to discover the etiology of eczema in infants and children. Their importance is not great during the first year of life. After the second year they are as important as foods. The patch test is not the correct test to use in testing with protein allergens. Protein allergens can act on the untraumatized epidermis, but this is unusual. Certain of them probably often act by contact if there is prolonged rubbing or slight trauma. They also act by inhalation. Contact dermatitis caused by nonprotein allergens is not common in infants and young children.

LATENT SYPHILIS. EDWARD W. KARCHER, New England J. Med. **213**:257, (Aug. 8) 1935.

In a paper written primarily for the general practitioner, the late Dr. Karcher aptly dwells on the great importance of individualization in the treatment of latent syphilis. In other words, therapy directed to the welfare of the patient and not simply toward eradication of a positive serologic reaction should be applied. Adequate but not excessive treatment is advised, and the choice of chemotherapeutic agents is discussed. Large doses of antisyphilitic preparations are deprecated. Complications and reactions to treatment are described. The value of examination of the spinal fluid is indicated. Latent syphilis and pregnancy receive just attention, and the importance of treatment in the face of circumstantial if not absolute evidence of syphilis to lessen the incidence of fetal infection is emphasized. A Wassermann-fast reaction is said not to be of serious import in the absence of clinical evidence of activity, but a close follow-up is advocated. Congenital latent syphilis is adequately discussed. It must be remembered that there is no positive test during life to determine cure or pathologic latency and that all patients who have had syphilis should be examined at least once a year throughout the remainder of their lives. The article is a well directed effort to guide the physician who only occasionally treats this disease.

LANE, Boston.

THE TREATMENT OF PSORIASIS WITH AN ORGANIC SULPHUR COMPOUND. FRANCIS M. THURMON, New England J. Med. **213**:353 (Aug. 22) 1935.

The article is a timely contribution to the contemporary revival of interest in colloidal sulfur. The preparation used by Thurman is a substance of uncertain composition (so common a character of the organic sulfur compounds) of which each cubic centimeter contains about 2 mg. of sulfur. This preparaton is used intravenously in doses of from 5 to 25 cc. and is apparently of low toxicity. Thurmon reports on fifty-eight patients of various ages suffering from different types of psoriasis. The results were "more gratifying" in the more extensive cases and less so in the milder cases. The article is a modest and reasonable presentation of a clinical study of a procedure proposed, not as a "cure," but as an addition to the armamentarium.

THE DIAGNOSIS OF INDUSTRIAL AND NON-INDUSTRIAL SKIN DISEASES. JOHN G. DOWNING, New England J. Med. **213**:358 (Aug. 22) 1935.

According to the Massachusetts Industrial Accident Board there were in the year ending June 1933, 410 cases of cutaneous disturbances among 96,144 cases of injuries reported. The highest incidence of cutaneous trouble occurred in leather and textile workers. Routine examination, frequent inspection and history of previous attacks are important in facilitating early detection. Latent periods between exposure and development of eruption vary from hours to years. The interpretation of the patch test presents the following difficulties: The reaction is variable; there are false positive and negative reactions; it is difficult to reproduce exact working conditions in the test. Epidermophytids and trichophytids may resemble industrial dermatitis. Dermatitis factitia frequently follows this condition in the period of readjustment.

APPEL, Boston.

A BACTERIOLOGICAL STUDY OF CERTAIN IMMUNE REGIONS IN SKIN LEPROSY. DANIEL G. LAI, Leper Quart. **9**:230 (June) 1935.

Lai states that Hopkins, Denny and Johansen pointed out the fact that areas which are not exposed to external irritants fail to show signs of leprosy. Among such protected sites are the axillae and the posterior inferior auricular area. Lai examined these areas bacteriologically and found the bacillus of leprosy about half as frequently in these protected sites as in contiguous areas of leprous skin of the same patients. The work of Hopkins and his associates was confirmed by the bacteriologic studies of Lai.

CIPOLLARO, New York.

INTERSTITIAL KERATITIS, BOOMERANG LEGS AND YAWS IN A EUROPEAN BOY FROM THE NEW HEBRIDES. C. J. HACKETT, M. J. Australia **2**:213 (Aug. 17) 1935.

Hackett reports in detail the case of a 14 year old boy who presented the symptoms of interstitial keratitis, saber-shaped tibias and yaws. The family history was carefully scanned for any positive evidences of congenital syphilis, and that factor was practically eliminated.

The author reviews the literature on the occurrence of interstitial keratitis and saber-shaped tibias with yaws. Saber-shaped tibias and yaws is found more frequently than interstitial keratitis and yaws. The concurrent occurrence of syphilis and yaws is rare; in fact, evidence shows that there is a cross-immunity between these two diseases. This condition responded rapidly to treatment with a brand of neoarsphenamine and potassium iodide and to inunctions of mercury. There was a prompt reversal of a 4 plus Wassermann reaction.

The author concludes that the symptoms were the result of yaws, because the history entirely eliminated the possibility of syphilis as an etiologic factor and the response to the treatment was so rapid.

BAER, Pittsburgh.

THE ETIOLOGY OF MYCOTIC DYSHIDROSIS. H. HRUSZEK, Dermat. Wchnschr. **100**:253 (March 2) 1935.

Following a burn of the tip of the thumb acquired at a public bath there developed a dyshidrotic eruption limited to the thumb. Cultural investigation showed the causative organism to be Achorion gypseum (Bodin). This organism does not, as a rule, give rise to a dyshidrotic lesion of the skin.

INDUSTRIAL STIGMA IN THE FORM OF A KERATOSIS FOLLICULARIS IN A LITHOGRAPHER. TADEUSZ CHORĄŻAK, Dermat. Wchnschr. **100**:255 (March 2) 1935.

A man aged 23 had worked in a lithographing shop for three months. An eruption consisting of keratotic hyperplasia around the follicular openings developed on the dorsa of the hands and on the lower two thirds of the forearms. The appearance simulated comedones. Histologic examination showed a widening of the follicular orifices with a horny plug. There was no inflammatory reaction.

ALLERGIC INVESTIGATIONS WITH BLASTOMYKIN (MIXED VACCINE AGAINST MYCOTIC INFECTIONS OF THE SKIN). ANDREAS DÓSA, Dermat. Wchnschr. **100**:258 (March 2) 1935.

Dósa made a mixed vaccine of various yeasts (Saccharomycetes, Oidium albicans, Monilia, etc.) by the Ballagi-Weisz method. By intracutaneous injections he obtained strongly positive reactions in patients with blastomycetic (yeast) dermatitis. In normal persons and in those with other cutaneous conditions only occasional and milder reactions occurred. Microsporin and favin caused no reactions in these persons while trichophytin occasionally caused a mild reaction.

REFUTATION OF CERTAIN OBJECTIONS TO GRENZ RAYS. B. SPIETHOFF and HEINZ BERGER, Dermat. Wchnschr. **100**:281 (March 9) 1935.

A number of authors have objected to the use of supersoft roentgen radiation in dermatology. Spiethoff and Berger have found these rays to be of considerable value, particularly in cutaneous conditions which are apt to recur frequently, such as eczema ani and psoriasis. They base their opinion on the relative safety of these rays as compared to that of ordinary roentgen rays, the difference being due to the lack of deep penetration of infra-roentgen radiation. Improvements in apparatus have removed the objections of clumsiness, small field of radiation and difficulty of accurately measuring the dosage.

EOSINOPHILIA IN LEPROSY. PAUL PARMAKSON, Dermat. Wchnschr. **100**:285 (March 9) 1935.

Parmakson studied the blood count of one hundred and three patients with various stages of leprosy. The results of his investigation were as follows: 1. Eosinophilia is not characteristically associated with leprosy. 2. In untreated patients with active stages of the disease there is a decrease in the number of eosinophils while in patients with latent stages there is a normal number or a slight increase. 3. In the course of successful treatment the number of eosinophils is increased.

PSORIASIS AND PYODERMA. O. WARTEMANN, Dermat. Wchnschr. **100**:289 (March 9) 1935.

Wartemann states that psoriasis does not in any way affect pyodermas and that it is not influenced by those conditions. He justifies this conclusion by describing briefly the cases of eight patients with psoriasis who suffered from various pyodermic disorders.

THE CLINICAL PICTURE OF VARIOLIFORM PYODERMA (PUSTULOSIS VARIOLIFORMIS ACUTA). V. BENDRE, Dermat. Wchnschr. **100**:305 (March 16) 1935.

A case of varioliform pyoderma occurring in a 28 year old man is reported. The patient had been successfully vaccinated several times and was not exposed to vaccine. Paschen bodies were not found in the lesions, but a pure culture of staphylococci was obtained. This organism is considered to be the etiologic factor. The literature is reviewed briefly.

BOWEN'S DISEASE. M. SCHUBERT, Dermat. Wchnschr. **100**:333 (March 23) 1935.

A case of Bowen's precancerous dermatosis is described in which a squamous cell epithelioma developed apparently as a result of a traumatic injury.

TAUSSIG, San Francisco.

ADENOMA SEBACEUM ASSOCIATED WITH A TUBEROUS SCLEROSIS OF THE BRAIN. VLASTA ŘÍHOVÁ, Česká dermat. **15**:201, 1935.

Říhová reports the occurrence of adenoma sebaceum in a girl aged 6 and in a boy aged 16 years. Both patients had epileptic seizures and a low mentality,

the boy being an imbecile. The parents of the girl were first cousins. Histologic examination revealed an atypical epithelial proliferation with long rete pegs and a hypertrophy of sebaceous glands; the corium had a rich blood supply.

Říhová considers adenoma sebaceum an organic nevus and an atavistic manifestation rather than a stigma of degeneration, a sort of example of the skin of a primitive man. In discussing the pathogenesis she expresses the opinion that an early damage of the embryonal ectoderm takes place, leading to the involvement of various tissues derived from the original layer: the central nervous system, the retina and the epidermis. Like nevi, this involvement may become manifest later during the postfetal life.

MYCOTIC INFECTION OF THE BUCCAL MUCOSA CAUSED BY LEPTOTHRIX. F. PATOČKA and J. OBRTEL, Česká dermat. **15**:206, 1935.

A healthy man, aged 36, with a good oral hygiene, presented on the floor of the mouth under the tongue a diphtheria-like, hard white, shiny membrane the size of a dime. There were several smaller satellite lesions. The surrounding mucosa showed no inflammatory reaction. There were no subjective symptoms except a slight salivation and a feeling as though a foreign body was present in the mouth. After two years of treatment the pseudomembrane showed a slight extension and no improvement.

Under strictly anaerobic conditions, two types of Leptothrix were isolated and grown in pure culture. As the organisms did not conform in their cultural characteristics to any known species, they were designated as type A and type B. Neither type was pathogenic for the animals into which they were inoculated. Antigen prepared from the cultures produced a negative intracutaneous reaction in the patient. Type A produced an inflammatory reaction in the controls.

SPINKA, Texarkana, Texas.

SUPERINFECTION AND REINFECTION OF RABBITS WITH SYPHILIS: II. NUMBER OF SPIROCHETES IN THE SPLEEN AND BLOOD OF SYPHILITIC RABBITS WHICH WERE SUPERINFECTED AND REINFECTED. K. SHIME, Lues: Bull. Soc. japon. de syph. **11**:223 (Dec.) 1934.

Rabbits were inoculated intracutaneously with spirochetes, and thirty-five and forty-five days later they were separated into two groups, one of which was to be superinfected and the other reinfected.

After a definite time a certain amount of blood and of material from the spleen was removed from these animals and inoculated intracutaneously into several areas of the back of a number of healthy rabbits.

The following observations were made: The period of incubation of the chancre produced by inoculation of emulsion of viscera of syphilitic rabbits is from five to nine weeks. These chancres are relatively small, are of varying size and involute rather quickly. The results of inoculation were much more frequently positive in superinfected than in reinfected animals.

The syphilitic rabbits which were superinfected with material from the spleen or with blood on the thirty-fifth day showed papules at the site of inoculation more frequently than those which were reinfected on the forty-fifth day.

Inoculation with material from the spleen gave a much stronger reaction than that with blood. A similar observation was made in the control animals. It is therefore to be assumed that there are many more spirochetes in the spleen of syphilitic rabbits than in their blood.

Metastases were produced in some rabbits by inoculation with material from the spleen but never by inoculation with blood.

The chancres produced in syphilitic rabbits by reinoculation with the material from the spleen were generally smaller if the emulsion was more diluted.

Rabbits which had been treated on the thirty-fifth day and then reinoculated showed a slightly less strong reaction than rabbits which had been treated on the forty-fifth day and then reinoculated.

STUDIES ON STAINING OF SPIROCHAETA PALLIDA, PARTICULARLY ON THE RELATION OF THE STAINING TO THE PREPARATION OF THE SLIDES. K. ONO, Lues: Bull. Soc. japon. de syph. **11**:247 (Dec.) 1934.

Ono has used fifty stains which are good for demonstration of Spirochaeta pallida in concentrations of 0.2 per cent and 1 per cent solutions.

The smears were fixed and prepared with dilute solution of formaldehyde, U. S. P. (1:10), 3 per cent solution of hydrogen peroxide or 1 per cent solution of potassium permanganate. Each of these three substances, used before staining, influenced favorably the staining of the spirochetes. The preparation with hydrogen peroxide is as useful for the fresh smears as for those fixed with the solution of formaldehyde. The slides fixed with the latter substance gave much better staining results when treated from five to fifteen minutes with 1 per cent solution of sodium bicarbonate.

In tables Ono enumerates the different staining substances, their concentration and the staining time for the following methods, which he recommends for the staining of S. pallida: (1) fixation with solution of formaldehyde, with or without subsequent treatment with sodium bicarbonate; (2) treatment of the smears with hydrogen peroxide with or without preceding fixation with solution of formaldehyde; (3) preparation with potassium permanganate, with or without fixation in solution of formaldehyde.

EFFECT OF INUNCTION WITH AN OINTMENT OF COLLOIDAL MERCURY IN HYDROUS WOOL FAT ON RABBITS INOCULATED WITH SYPHILITIC MATERIAL. H. KO, Lues: Bull. Soc. japon. de syph. **11**:268 (Dec.) 1934.

Ko has investigated the effect of inunctions with an ointment of colloidal mercury in hydrous wool fat in syphilitic rabbits. Inunctions were given on six successive days, with from 0.14 to 0.15 Gm. of a 19 to 20 per cent concentration of the aforementioned preparation, which contained from 4 to 5 per cent of bismuth. After an interval of two days the six daily inunctions were repeated, and six such courses were given; this constituted a complete course of treatment.

In two rabbits this treatment was started four days before they were inoculated with an emulsion of spirochetes. A third rabbit was used as a control. Inunctions prevented the development of chancres at the sites of inoculation. Twenty-one days after the first complete course of treatment the spleen and lymph glands were removed and inoculated into other rabbits. The result of the inoculation was negative.

In a second experiment the treatment was started after the chancre had developed. Ten daily inunctions caused the disappearance of the chancre. One rabbit showed a relapse fifty-one days after the first complete course of treatment. Another rabbit died sixty-eight days after the first course.

Inoculation with material from the spleen and lymph glands removed from rabbits sixty-eight days after the second course gave negative results.

The second course of treatment brought about the cure of the papular eruption caused by the relapse. One hundred and thirty-three days after the inoculation no signs of syphilis could be seen in the treated rabbits, but the control animal showed large rupioid chancres.

Inunctions were given to two rabbits, the course of treatment starting one day before the animals received intravenous inoculations with spirochetes. In one rabbit a papular eruption, which gradually extended, developed thirty-one days after the first course of treatment. In the second rabbit no sign of syphilis developed after the first course of treatment, and inoculation with material from the spleen and lymph glands gave a negative result. The control animal showed a papular eruption twenty-six days after the intravenous inoculation, and on the forty-sixth day orchitis and papules on the scrotum appeared.

Three rabbits received inunctions from the thirty-fourth day after the intravenous inoculation. The papules started to recede soon after the beginning of

the treatment, and after ten days they had almost entirely disappeared. On the thirty-second day after the first course of inunctions the spleen and lymph glands were removed from these animals and material from these organs was inoculated into healthy rabbits; the result was negative.

Ko concludes that the therapeutic effect of inunctions with an ointment of colloidal mercury in hydrous wool fat is efficient, but he thinks that one course of treatment is insufficient to eradicate the infection.

SUPERINFECTION AND REINFECTION OF RABBITS WITH SYPHILIS: III. SPIROCHETE CONTENT OF THE BLOOD OF INTRAVENOUSLY REINFECTED RABBITS. K. SHIME, Lues: Bull. Soc. japon. de syph. **12**:1 (Feb.) 1935.

Rabbits which had been infected with spirochetes thirty, a hundred and sixty-three, a hundred and ninety-five, four hundred and eighty-eight or six hundred and thirty-six days previously, were treated thoroughly with a brand of arsphenamine, and seventeen, twenty-two and forty-three days later they were reinfected intravenously. Thirty-five, thirty-six or forty days after the animals had been reinfected blood was taken from them and inoculated in different dilutions intracutaneously into normal rabbits. The blood taken from rabbits which received treatment later than a hundred and sixty-three days after the primary infection produced a negative reaction.

The blood of two animals in which treatment was started thirty days after the first infection and which had been reinfected intravenously seventeen days later produced a positive reaction thirty-six days after reinfection.

These experiments show that rabbits with an old syphilitic infection have increased resistance against the intravenous inoculation with Spirochaeta pallida. The animals which are reinfected at an early period after the primary infection do not show any increased resistance against intravenous reinoculation.

BLOOM, New York.

CHANGES IN SKIN NERVES IN PELLAGRA. M. A. ROSENTOUL, Acta dermat-venereol. **15**:495 (Dec.) 1934.

In the initial stage of pellagra there is a considerable irritation of the peripheral nervous system (spindle-shaped swelling of fibers, defibrillation, etc.). This irritation seems to be responsible for the marked impregnation with silver of the nervous fibers. There is a secondary degeneration of the latter, and the findings are similar to those in cases of toxic neuritis, chronic lead poisoning, rice neuritis and beriberi. Rosentoul favors the alimentary theory of the etiology of pellagra.

DIFFUSE CUTANEOUS MANIFESTATIONS IN MALIGNANT LYMPHOGRANULOMATOSIS. Z. CZEŻOWSKA and H. MIERZECKI, Acta dermat.-venereol. **15**:501 (Dec.) 1934.

A case of malignant lymphogranulomatosis with involvement of the pleura, mediastinal and other lymphatic glands is described. The diagnosis was confirmed by a biopsy. The cutaneous manifestations in this case consisted of superficial, painless ulcerations regularly scattered all over the body and extremities without any tendency to confluence. The cutaneous eruption was accompanied by lesions in the mouth, which resembled those of the skin, except that they were less intense. The ulcers situated on the upper extremities and on the thorax disappeared after roentgen irradiation of the mediastinal glands. The ulcerations on the lower extremities disappeared after irradiation of the abdomen. All these ulcerations reappeared when the general condition of the patient became worse, as manifested by enlargement of the mediastinal tumor, elevation of the temperature, etc. There was, however, one ulceration in the region of the left tibiotarsal articulation which grew in size and was not influenced by the roentgen irradiation. A biopsy specimen taken from this lesion showed the presence of Sternberg's cells.

THE PROBLEM OF HYPERSENSITIVITY. S. K. ROSENTHAL, Acta dermat.-venereol. **15**:514 (Dec.) 1934.

Rosenthal describes a case of scarlatinoid eruption which appeared a few days after the ingestion of mild mercurous chloride and after an intense irradiation with the rays of the sun. The eruption was present on the face and trunk and all the extremities except the lower left one, which was almost free from involvement. According to Rosenthal, the cutaneous reaction on the lower right extremity may be explained by the fact that the patient had a fracture of that limb a few years before, at which time the limb was immobilized for three months. Rosenthal considers the exposure to the solar rays and the history of trauma in this case as nonspecific factors in the pathogenesis of hypersensitivity. He believes that nonspecific factors may change conditions in such a way that perfectly harmless substances may cause a primary reaction in the human body. A real state of hypersensitivity may develop respectively during and after the aforementioned primary reaction.

CASE WITH THE DIAGNOSIS: SALVARSANENANTHEMA (SALVARSAN-BISMUTH-ENANTHEMA). INGEBORG KJELLIN, Acta dermat.-venereol. **15**:525 (Dec.) 1934.

Kjellin describes the case of a woman, who, after receiving an injection of a brand of arsphenamine became ill with severe pains and marked tenderness in the abdomen, vomiting and a rapid and weak pulse rate. Because ileus was suspected a laparotomy was performed. The abdominal cavity was found to be filled with a clear yellowish fluid, and a considerable part of the small intestines was reddened and edematous. The patient recovered. Because of the fact that the patient showed a hypersensitivity to arsphenamine Kjellin believes that this case should be considered as one of an urticarial type of exanthema of the intestines or enanthema due to arsphenamine. It is impossible to decide whether the treatment with bismuth played any etiologic rôle.

ASTRACHAN, New York.

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

HENRY SILVER, M.D., *Secretary*

Regular Meeting, March 28, 1935

LOUIS CHARGIN, M.D., *President*

IDIOPATHIC MULTIPLE HEMORRHAGIC SARCOMA (KAPOSI). Presented by DR. G. D. ASTRACHAN.

J. G., a man aged 52, born in Italy, came to the dispensary of the Metropolitan Hospital because of an eruption on the feet and legs which had been present for six years. In 1934 the patient was confined for a time to the Metropolitan Hospital, where he received six roentgen treatments, which resulted in improvement of the condition.

The eruption on the soles, dorsa of the feet and lower part of the legs is composed of scattered elevated lesions from the size of a pinhead to that of a pea; some of the lesions are indurated and present sizable nodules. On the lateral aspect of the right foot and on the medial side of the left foot are well defined, irregularly shaped, somewhat elevated reddish-blue palm-sized infiltrated plaques, the borders of which are dark blue and indurated. A light brown papular infiltrated lesion is present on the volar side of the base of the left thumb. The patient complains of intense pain and stinging sensation in the feet. The Wassermann test of the blood and the examination of the blood and urine gave negative results. The results of the biopsy corroborated the clinical diagnosis of Kaposi's sarcoma.

DISCUSSION

DR. G. D. ASTRACHAN: The lesions on the feet are fairly typical of Kaposi's sarcoma, and this diagnosis is sustained by the results of the biopsy. It is doubtful whether the pea-sized elevated light brown lesion which is seen on the base of the thumb is likewise a Kaposi sarcoma.

DR. DAVID L. SATENSTEIN: I wish to discuss only the lesion on the hand because of a similar lesion seen by most of the members at the meeting of the New York Academy of Medicine. The case to which I refer is that of a dentist who had a rather widespread case of Kaposi's sarcoma. Lesions developed on the dorsa of the hands and on the body, and one lesion appeared in the larynx, but the biopsy proved these lesions to be nevocarcinomas. About forty lesions were removed, and the operation was followed by roentgen irradiation, but in the end amputation of the hand had to be resorted to. The lesion on the hand of Dr. Astrachan's patient may be of a similar character.

DR. VAN ALSTYNE H. CORNELL: I saw the patient when he first came to the hospital, and I can state that considerable improvement occurred in the lesions after the use of six doses of ¼ unit (75 roentgens) of unfiltered roentgen radiation.

DR. DAVID BLOOM: A few years ago I presented at a meeting of the New York Academy of Medicine a patient with an early stage of Kaposi's sarcoma; the condition cleared up under roentgen therapy, and no recurrence has taken place. I believe that such treatment given at an early stage of the disease is effective.

DR. SAMUEL FELDMAN: In connection with Dr. Bloom's remarks I wish to cite the case of the patient with lesions in the mouth whom I presented before this society. The patient was subjected to radium therapy and is apparently cured.

DR. DAVID L. SATENSTEIN: Regarding therapy, I wish to state that I doubt whether treatment with roentgen rays or radium is effective as a curative measure.

DR. G. D. ASTRACHAN: The lesions under discussion developed in the last three months, and in view of Dr. Satenstein's remarks I shall make a biopsy of the lesion on the hand.

LICHENOID ERUPTION OF SECONDARY SYPHILIS. Presented by DR. F. E. CROSS.

J. G., a man aged 52, presents an erythematopapular eruption on the abdomen, chest, face and scalp. The lesions are flat, shiny and polyhedral; some are covered with a fine adherent scale, and they vary in size from that of a pinhead to that of a bean. On the anterior aspect of the upper part of the chest there are several annular lesions. The lesions on the face, forehead and scalp are more flat; they are shiny and coalesce. The lesions on the glans penis are flat, shiny and covered with scales. There is no itching, and the eruption lacks the characteristic violaceous or lilac color of lichen planus and has a more brownish tinge. The pathologic examination revealed a thinning of the epidermis caused by the presence of a large mass situated just below the epidermis and extending to the lower portion of the cutis. This nodule was composed of epithelioid cells and Langhans giant cells with few lymphocytes. The histologic picture suggested lichen scrofulosorum. Lichen planus could be definitely ruled out. The Wassermann reaction of the blood was 4 plus.

DISCUSSION

DR. SAMUEL M. PECK: The clinical diagnosis submitted with the specimen of tissue for histologic examination justified a diagnosis of lichen planus. Histologically, however, the picture was that of lichen scrofulosorum, with the exception that there was not as much perifollicular involvement as is usually seen in cases of the latter condition. Authorities agree that the histologic picture of a lichenoid eruption due to syphilis and that of lichen scrofulosorum may be identical.

DR. G. D. ASTRACHAN: This patient presents on the arms and back lesions which look like a lichenoid follicular manifestation of syphilis. However, the lesions on the upper part of the chest resemble lichen planus. Therefore, the diagnosis of secondary syphilis can be made only with reservation.

DR. VAN ALSTYNE H. CORNELL: The patient is 64 years of age. He has had the eruption for four weeks. There is no sign of a primary lesion anywhere. I believe it was mentioned that there were no lesions of lichen planus, but I do not hesitate to state that the patient does show shiny papules of lichen planus. I was therefore convinced that the condition was lichen planus until I saw the reports of the biopsy and of the Wassermann test. I reexamined the patient, and I am now of the opinion that there is a mixture of lesions. I do not know which diagnosis to favor.

DR. EUGENE F. KELLEY: Has this patient received antisyphilitic treatment? It is well known that an eruption resembling lichen planus can occur after injections of arsphenamine.

DR. DAVID L. SATENSTEIN: The patient presents a widespread eruption which appeared suddenly. It follows the lines of cleavage posteriorly, and the lesions are shiny and reddish. Around the clavicular zone they are edematous. Careful examination reveals fine scales topping many lesions. I do not think that the diagnosis of lichen planus should be favored. The histologic picture does not quite fit in with the diagnosis of lichen scrofulosorum, as Dr. Peck suggested. I accept the diagnosis of secondary syphilis.

DR. DAVID BLOOM: I agree with the diagnosis of secondary syphilis. The lesions on the penis do not look like lichen planus. The atypical picture of the lesions on the trunk is produced particularly by the coalesced scaly patches. Such

patches are seen from time to time in eruptions due to secondary syphilis. In view of this evidence and of the positive Wassermann reaction the diagnosis as given by the presenter is justified.

DR. PAUL GROSS: The combination of a typical secondary eruption of large papules with lichen syphiliticus is unusual.

DR. C. LERNER: The reason that the diagnosis of lichen planus suggests itself strongly at first glance is that the smaller lesions are closely packed and, being situated over convex tense areas such as the clavicle, they appear shiny. The lesions on other parts of the body, where the skin is not stretched, certainly do not resemble those of lichen planus.

DR. MAURICE UMANSKY: This patient presents several varieties of lesions at the same time. Lesions covered with scales suggesting psoriasis are visible on the upper portion of the chest. Lesions resembling sarcoid are disseminated among papules of other types. The polymorphism of the eruption makes the diagnosis of syphilis more probable.

DR. F. E. CROSS: When the patient was first seen at the clinic my co-workers and I thought we were dealing with a rare type of lichen planus involving the face and scalp. Further observation inclined us to favor a possible diagnosis of tuberculosis, but the duration of the condition seemed opposed to this diagnosis. When the study of the case was completed it was agreed that the disorder was a lichenoid manifestation of syphilis. The result of the biopsy in this case is important, and though it did not establish a positive diagnosis, at least it ruled out lichen planus histologically. Against the diagnosis of lichen planus the following points should be mentioned. 1. There was no itching. 2. In cases of lichen planus one rarely observes an involvement of the face and scalp. 3. The color was not that of lichen planus. The lesions are brownish red instead of being violaceous. The duration of the eruption, the positive Wassermann reaction, the results of the biopsy and the color certainly fit in well with the diagnosis of a lichenoid manifestation of syphilis.

CHRONIC URTICARIA WITH SPECIAL REFERENCE TO ETIOLOGIC FACTORS. Presented by DR. MARION B. SULZBERGER for DR. ADOLPH ROSTENBERG JR.

M. P., a woman aged 19, a stenographer, first came to the clinic for allergic disorders of the skin of the French Hospital on March 1, 1935. She states that she has had urticaria for the past three years. The attacks occurred nearly every day but were more severe during the winter.

The patient's mother is suffering from hay fever. There are no other relevant features in the patient's personal or family history. She has received various medicaments by mouth for the urticaria, but no appreciable benefit has resulted. Scratch tests with dried protein extracts gave the following results: Strongly positive reactions were obtained with crab meat, egg white, chicken feathers, duck feathers, dog hair, rabbit hair, cattle hair, horse dander, sheep wool, silk and cotton; positive reactions were obtained with hops and cat's hair. A dubious reaction was obtained with orris; negative reactions were obtained with buckwheat, beef, codfish, corn, barley, chicken, coffee, egg yolk, herring, cow's milk, orange, pork, rice, string beans, wheat, lamb, mackerel, potato, rye, shrimps, tomato, tobacco, Pyrethrum, kapok and flaxseed. Passive transfer experiments made according to the method of Prausnitz and Küstner gave the following results: egg white, 1:10 dilution, negative; egg white, concentrate, negative; mixed epidermals, 1:100 dilution, 1 plus; orris concentrate, 2 plus; silk, 1:100 dilution, negative; crab meat, 1:500 dilution, 1 plus.

The hope that this presentation might throw some light on either the etiology or the therapy of chronic urticaria is likely to prove ungratified. On the contrary, the causes and therapy of urticaria may be more incomprehensible. It is by no means proved that the presence of passive transfer antibodies is significant as far as the clinical etiology of a condition is concerned. Both the positive cutaneous

tests and the findings of specific reagins cannot be considered as establishing an etiology unless they can be corroborated by clinical evidence and therapeutic tests. And this criticism applies to all forms of cutaneous tests.

DISCUSSION

DR. SAMUEL M. PECK: I used to be more optimistic than I am at present about testing the skin of patients with chronic urticaria. Only rarely does one obtain a clue to the real etiologic factor from such a procedure, even if hundreds of tests are made. Of course, if the patient's economic status permits, such a procedure may be justified, and even then in private practice it is only fair to tell the patient that the results are uncertain. The history is probably much more important than the cutaneous test. In the last analysis one must proceed to nonspecific methods, such as diets which reduce cutaneous sensitivity, autochemotherapy, etc.

DR. ARTHUR SAYER: I know of one instance in my own family worth reporting. Examination of the blood and other chemical examinations yielded no results. The allergist made a complete series of cutaneous tests, about fifty of which were positive. On further consultation I was advised that when a person is sensitive to one or two substances or to a group of substances the positive tests are of diagnostic significance but that if a patient shows positive reactions to many different substances the tests are not of much practical value. As far as diet is concerned, I do not think that it should be restricted in cases in which the patient exhibits many positive reactions. In spite of severe restrictions of diet my patient was not benefited. However, after two or three years the urticaria finally improved, and the patient remained free for one year. I wish to emphasize the fact that if the tests are positive for a great variety of foods, inhalants, etc., as in this patient's case, the reactions should not be considered of much significance from the etiologic or from the therapeutic point of view.

DR. PAUL GROSS: I should like to know how Dr. Sulzberger explains the positive reactions and positive passive transfers in these cases in the presence of many negative reactions. If the reactions were all positive one could attribute that to a peculiar reaction of the patient's skin, but the selective positive reactions must mean something even if they do not shed light on the etiology. In my own practice I have found that by carrying out careful elimination diets in cases of eczema and chronic urticaria I could usually dispense with cutaneous tests, but of course a great deal of patience and a careful taking of the history are necessary. In cases of chronic urticaria I find it important to give immediate treatment which will subdue the urticarial reaction. Equally important is a thorough search for foci of infection, as Dr. Hopkins has shown. There are also cases in which the focal infection acts as a sensitizing agent for other allergens. It is helpful to make a strict differentiation between chronic urticaria and recurrent urticaria since the latter can more frequently be traced to a specific food.

DR. F. E. CROSS: I agree in the main with Dr. Peck's remarks and should like to add that two factors play an important rôle in cases of chronic urticaria: gastro-intestinal and neurogenic disorders. I have observed an interesting example of the latter etiology in my practice: A woman had an attack of chronic urticaria each time her husband indulged in excessive drinking.

DR. MARION B. SULZBERGER: I completely agree with the previous speakers and particularly with Dr. Peck. The cutaneous tests should be considered from two different points of view: 1. As means for finding the specific etiology. From this point of view patch tests when employed in cases of contact dermatitis are the only ones of significance in the usual dermatologic cases. 2. As a help in the study of urticaria in general and of the significance of cutaneous tests in general.

It is my opinion that positive urticarial reactions to cutaneous tests (even if there are forty positive and forty negative reactions) indicate that the patient's

skin is hypersensitive to the substances eliciting the positive reactions when applied by cutaneous tests (provided, of course, the technic has been correct and proper control tests have been made). In a certain proportion of such positive tests one can demonstrate real immunologic sensitivity by demonstrating passive transfer. However, as yet it is not known what these positive tests, or even what reagins, mean as far as their clinical significance, i. e., as far as the etiology of the urticaria, is concerned. If the patient is sensitive to orris, silk and inhalants as well as to eggs, it certainly cannot be hoped that the condition will be cured by the removal of eggs from the diet. In order to study such cases not only is it necessary to go through exhaustive tests but there must be rigid eliminations not only of dietary constituents but also of environmental and inhalant allergens. But even the food and inhalants may be but concomitant factors in this case under consideration, and there may be a focus of infection that sensitizes this patient. Hence one can recognize how impossible it is at present to come to a conclusion regarding the clinical significance of the cutaneous tests.

In general, I may state that I believe that foci of infection and drugs are two of the most important factors in cases of chronic urticaria. Drugs must be absolutely eliminated before one begins the further investigation of any case of long standing.

DR. DAVID L. SATENSTEIN: What value has testing from a purely clinical standpoint in the control of the itching, which is so troublesome a symptom?

DR. MARION B. SULZBERGER: From the standpoint of helping the patient the value of cutaneous tests consists in the possible finding of the etiology and in the resultant cure of the disease.

DR. ADOLPH ROSTENBERG JR.: Calcium is used with varied results. Abroad large doses are given, i. e., 10 cc. of a 10 per cent solution intravenously three times a day and also 2 tablespoonfuls by mouth. Are the results better than those obtained by other means?

DR. MARION B. SULZBERGER: I do not think that the larger doses of calcium give better results than smaller ones. I have given calcium by daily injections of a 10 per cent solution of calcium gluconate in addition to oral administration of calcium gluconate. The administration of such large doses sometimes produced hypercalcemia without benefiting or altering the course of the chronic urticaria.

ERYSIPELAS-LIKE DERMATOPHYTID. POSITIVE IMMEDIATE WHEAL REACTION WITH TRICHOPHYTIN REAGINS. Presented by DR. MARION B. SULZBERGER.

C. W., a furrier aged 52, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital was presented before the New York Dermatological Society by Dr. Eugene Traub on March 26 (ARCH. DERMAT. & SYPH. **33**:196 [Jan.] 1936).

DISCUSSION

DR. MARION B. SULZBERGER: Dr. Traub, who presented this patient before the New York Dermatological Society, was convinced that the erysipelas-like eruption was a reaction to the products of fungi from foci on the feet and was therefore an "id." However, this patient showed a negative reaction to tests with trichophytin and oidiomycin at sites at which other patients would be sensitive according to the usual method of reading the reactions, that is, if one considered only the characteristic reaction occurring in from twenty-four to forty-eight hours. The patient was then retested, a test with trichophytin being made on one leg and a test with oidiomycin on the other. Within ten minutes there was around the site tested with trichophytin a hot, edematous, erythematous area the size of a small palm which exactly simulated the spontaneous lesion on the dorsum of the foot. There was no reaction to the test with oidiomycin. Tests with trichophytin made on the arm immediately produced strong wheals and flare reactions, while the forty-eight hour reaction was again negative. Tests with oidiomycin

were all negative. This patient has strong reagins (passive transference antibodies) to trichophytin in his serum; such reagins were found in the two patients whose cases I have previously reported (*J. Allergy* **2**:11, 1930; *J. A. M. A.* **95**:1504 [Nov. 15] 1930). There were no reagins to oidiomycin or streptococcus extracts. I consider this condition to be a type of interstitial and inflammatory, edematous and erysipelas-like dermatophytid appearing near the focus and produced by the products of the fungi.

DR. SAMUEL M. PECK: Dr. Sulzberger is to be congratulated on his point of view in this case. There are a number of unusual complications of dermatophytosis between the toes. It is not uncommon to see a traveling phlebitis accompanying a ringworm infection of the foot. Patients with such a condition tend to have recurrences and may show an elevation of temperature. Surrounding an area of phlebitis one may see an erysipelas-like cellulitis. Another complication, occurring especially in diabetic patients, is a rapid breakdown of tissue to form superficial ulcerations.

I have observed an unusual complication in a middle-aged woman who had attacks of burning sensation in the feet accompanied by swelling and redness of the legs. These attacks of dermatosis were followed by epileptiform convulsions. Examination of the lesions on the feet revealed fungi. A test with trichophytin gave the delayed type of reaction, and in forty-eight hours the patient had another epileptic seizure. In order to determine whether there was any connection between the reaction and the seizure I gave the patient 1 cc. of a 1:100 dilution of trichophytin intramuscularly, whereupon a marked focal flare-up with edema and redness appeared on the lower portion of the legs, and in about forty-eight hours the patient had another epileptiform attack. When that attack subsided she had an erysipelas-like eruption on both legs and had to be confined to bed for a week. A thorough attempt was made to clear up the fungous infection of the feet, and the patient was seen regularly for about one and one-half years. During that time her neurologic symptoms have not manifested themselves. Recently she had a recurrence of the dermatophytosis. This was again followed by cellulitis of the leg and an epileptiform attack. She was taken to the Mount Sinai Hospital, and trichophytin was given intramuscularly as before, but this time the neurologic symptoms could not be elicited. I interpreted this case as one of possible vascular sensitization to fungi or their products; such a sensitization might have accounted for the neurologic symptoms.

DR. C. LERNER: What, if any, control test did Dr. Sulzberger use on the other leg? Did he rule out any primary vascular disease, including an ascending phlebitis? Is it not possible that the patient presented is sensitive to the dyed socks?

DR. MAURICE UMANSKY: The positive reaction to trichophytin indicates a causal connection between the dermatophytosis and the erysipelas-like dermatitis. The treatment and eventual cure of the dermatophytosis should prevent recurrences of the erysipelas in this case.

DR. MARION B. SULZBERGER: Dr. Traub and Dr. Williams intend to report a series of these cases, which they have been investigating. I present this patient with the diagnosis of erysipelas-like dermatophytid. If Trichophyton can produce an urticarial wheal type of reaction and can elaborate an antigen which produces specific reagins, theoretically it may cause vasomotor rhinitis, asthma and other reactions of such an explosive and shock type, for instance, as Dr. Peck has said, epileptic seizures. Several years ago I was able to demonstrate the existence of states resembling asthma and hay fever due to trichophytin. With the reagins of these patients I demonstrated that Trichophyton, Microsporon and Achorion bear a certain immunologic relationship to each other, while Monilia is apparently outside of this immunologic group; that is, the monilias (oidiomycin) contained no antigen capable of reacting with the specific reagins of Trichophyton (*J. Immunol.* **23**:73, 1932).

CHANCROID AND LYMPHOGRANULOMA INGUINALE WITH BUBOES. Presented by DR. DAVID BLOOM.

In J. E., a Negro aged 26, there developed in January 1935 an ulcer on the prepuce, just behind the sulcus coronae; it lasted for about four weeks. One week after the appearance of this ulcer a swelling appeared in each inguinal region. On the right side it reached the size of an orange, and on the left, that of a hen's egg. At the same time swellings the size of an almond developed on the left posterior aspect of the distal portion of the penis. Pus was aspirated and some "burning liquid" was injected into the inguinal swellings, which remained, however, unchanged.

The patient exhibited positive reactions to the Frei and to a stabilized streptococcus antigen. Pus removed from the swellings at the distal end of the penis and prepared in the usual manner yielded a good Frei antigen. The Wassermann reaction of the blood was plus-minus. The patient said that he had a positive Wassermann test in September 1934. He had received a few intramuscular and intravenous injections.

DISCUSSION

DR. MARION B. SULZBERGER: This is an interesting case. I have seen a few such swellings of lymphatics on the dorsum of the penis in cases of lymphopathia venerea.

DR. SAMUEL FELDMAN: Because of a recent experience I should like to hear Dr. Bloom's opinion about the specificity of the Frei test. A patient had large masses which filled up the entire abdomen. He also had large glands in the neck and in the groin. Clinically no one would have hesitated to make a diagnosis of abdominal cancer, yet the condition was diagnosed elsewhere as lymphogranuloma inguinale because the Frei test was positive.

DR. DAVID BLOOM: From my own experience and from what I have read on this subject I consider the test specific. I had the opportunity to see at the gynecologic department of the Bellevue Hospital patients with stricture of the rectum associated with pelvic tumors who gave positive reactions to the Frei test. I am sure that a great number of adnexal tumors are due to the virus of lymphogranuloma inguinale. The swellings at the distal end of the penis are analogous to the buboes of lymphogranuloma in the inguinal region, for the pus removed from one of them yielded a strong Frei antigen. This is the second case of this kind that I have observed.

LEUKODERMA CENTRIFUGUM ACQUISITUM (SUTTON). Presented by DR. SAMUEL FELDMAN.

R. DeS., a housewife aged 28, states that she has had the condition of the skin as long as she remembers. There are two sharply defined depigmented areas presenting a somewhat elevated light brown spot in the center. The larger lesion, which measures about ¾ by 1½ inches (1.9 by 3.8 cm.) in diameter, is situated on the left side of the trunk, and the central spot is about as large as a good-sized pea. The lesion on the back is smaller, and the central pigmented spot is also smaller. The patient has cardiac disease. All laboratory examinations gave negative results. The pathologic changes characteristic of this disease as Sutton describes them are confusing. It is difficult to understand the statement that the cutis is infiltrated with endothelial cells.

DISCUSSION

DR. DAVID L. SATENSTEIN: What Sutton described is an intracutaneous nevus. Other pathologists refer to such nevi as endothelial cells.

HENRY SILVER, M.D., *Secretary*

Regular Meeting, April 25, 1935

LOUIS CHARGIN, M.D., *President*

EXTENSIVE ERYTHEMA NODOSUM. Presented by DR. CHARLES WOLF.

T. B., a boy aged 15, states that he struck the left leg two weeks ago. Soon after the accident an erythematous lesion appeared on the left shin. Lesions then developed on the remaining portion of the leg anteriorly and posteriorly and spread to the thigh. The right lower extremity became involved a few days later and the forearm about one week later. The lesions are discrete tender red nodules; some are confluent.

DISCUSSION

DR. MARION B. SULZBERGER: This is certainly an erythema nodosum-like eruption. One must, however, consider the direct etiology. In my experience halogens are not infrequently the cause of such dermatoses. Tincture of iodine had been freely used on a large abraded area over the tibia shortly before the nodose erythema appeared. I have seen eruptions similar to this resulting from the ingestion of bromides and iodides and from the external application of tincture of iodine. In the absence of tonsillitis or tuberculosis the possibility of an erythema nodosum-like eruption due to iodide must be considered.

DR. PAUL GROSS: This condition is typical erythema nodosum, which clinically is better described as contusiform. I have seen several cases of extensive erythema nodosum due to bromides and one case in which the condition was due to iodides, but in this patient the condition is probably due to acute infection.

DR. ADOLPH ROSTENBERG: I believe that clinically this is a case of erythema nodosum. The possibility of an eruption due to a drug should, however, be considered. I saw a similar eruption which, as I was able to demonstrate, was due to quinine.

DR. EUGENE F. KELLEY: One point has not been stressed, that is, the elevation of temperature; this may rule out an eruption due to a drug.

DR. SAMUEL FELDMAN: I do not regard this eruption as caused by a drug. One cannot disregard the view expressed in the foreign literature that erythema nodosum is a tuberculous manifestation. In this case the evidence suggestive of pulmonary tuberculosis is quite strong.

DR. LOUIS CHARGIN: In the Scandinavian countries it is generally accepted that erythema nodosum in young patients is of tuberculous origin. This view is based on clinical as well as on roentgen and biologic evidence.

DR. ARTHUR SAYER: In a recent article on erythema nodosum (H. J. Ustvedt and A. S. Johannessen, *Acta med. Scandinav.* **80**:262 [Sept.] 1933) the authors stressed the point that erythema nodosum is an allergic manifestation of tuberculosis. The incidence of pulmonary tuberculosis in adults in the group observed was stated to be about 14 per cent. The authors found that signs of pulmonary tuberculosis developed in 10 per cent of the patients during the first year and that about 4 per cent manifested signs of tuberculosis before the end of the fifth year.

A CASE FOR DIAGNOSIS (PEMPHIGUS?). Presented by DR. LOUIS CHARGIN.

This man, aged 28, has been suffering from a cutaneous condition which has been limited to the posterior aspect of the neck and adjacent regions of the shoulders for about five years. About two years ago he was free from eruption for six months. The process is eczematoid, with a more or less sharp border. On

repeated observation it was discovered that it begins with small bullae which appear chiefly at the border of the eruption and that thus the process advances. While new lesions appear the old ones heal and the affected area, while limited to the neck, shows a different configuration when the patient is seen at weekly intervals. The patient states that he has taken no drugs except a remedy for colds or medication for the bowels occasionally, but this does not seem to aggravate the condition. The process does not appear to be pemphigus, multiform erythema or dermatitis herpetiformis. The subjective symptom consists of slight itching; except for this disorder the patient is in good health.

DISCUSSION

DR. ADOLPH ROSTENBERG: The condition in this patient strikingly resembles that in one under my observation except that in my case the lesions are more extensive. My patient had the disorder for five or six years, during which it was recurrent. My diagnosis was eczema, and I found that the process responded to a single roentgen treatment (75 roentgens unfiltered). I have tried to eliminate local irritations by insisting that the patient wear soft collars or entirely eliminate wearing collars, but without success. I was unable to determine the etiologic factor in spite of diligent efforts.

DR. PAUL GROSS: There is a striking resemblance to the lesions in the Senear-Usher type of pemphigus. Since there is still little known about this syndrome, one can well assume that the process can behave as it does in this patient.

DR. HENRY SILVER: I agree with Dr. Gross that this condition may be the Senear-Usher type of pemphigus. The striking similarity of the heavily crusted lesions, the tendency to creep upward, the healing without leaving atrophy and the frequent recurrence are in favor of that diagnosis.

It is unnecessary to stress that one roentgen treatment benefited the condition. The lesions have a tendency to clear spontaneously.

DR. DAVID BLOOM: I have seen frequent references to localized dermatitis herpetiformis in the German literature. I believe that this diagnosis may well be considered in this case.

DR. ISIDORE M. LASHINSKY: I agree with Dr. Gross' suggestion of a Senear-Usher syndrome. If the disorder is considered to be a type of lupus erythematosus, I suggest therapy with a gold preparation.

DR. MARION B. SULZBERGER: I think it is sometimes difficult to rule out dermatitis venenata, but I am sure that Dr. Chargin has done so. However, one is never through investigating possible causes in a case like this. If contact dermatitis can be ruled out I should consider dermatitis herpetiformis as a possible diagnosis.

DR. LOUIS CHARGIN: The most likely diagnosis is an unusual form of multiform erythema. The bullous lesion, associated with erythema and exhibiting an advancing border, seems to suggest this diagnosis. Unless the disorder is a limited form of dermatitis herpetiformis, this diagnosis must be ruled out. I feel reasonably certain that the condition is not an eruption due to a drug and that it is not a dermatitis artefacta. Even if it is pemphigus, I cannot accept the suggestion that it is of the Senear-Usher type.

KERATOSIS PALMARIS ET PLANTARIS. Presented by DR. SAMUEL FELDMAN.

T. N., an American girl aged 7½ years, of Greek parentage, came to the Morrisania City Hospital on April 24, 1935, presenting hard horny plaques on the palms and soles. The condition appeared about six years ago when the child began to walk.

There are circumscribed waxy, translucent horny masses, ranging in size from that of a hazelnut to that of a small hen's egg, on the heels, metatarsal arches and balls of the big toes. The palms are somewhat hard, and a few minute horny

lesions can be discerned. It appears that the areas subjected to pressure are mostly affected.

The patient's father, who was born in Sparta, Greece, has had a similar condition of the palms and soles since he was 1½ years old. A brother of the patient, who is 4 years old, has had a similar condition since he began to walk. There is no consanguinity in the family.

DISCUSSION

DR. PAUL GROSS: The interesting feature in these three patients is that the father has keratoma palmare dissipatum and a more diffuse type on the soles. It is generally accepted that the disorder known as mal de Meleda and hereditary keratoma palmare and plantare is one and the same process.

DR. DAVID BLOOM: I presented this patient and her father before the Section of Dermatology and Syphilis of the New York Academy of Medicine (ARCH. DERMAT. & SYPH. **25**:1123 [June] 1932). The father, who is a shoemaker, had a number of striated and papular keratotic lesions on the palms and fingers and a few plaques on the heels and balls of the feet. The girl had a few small plaques on the heels and toes. Now there are keratotic lesions on the soles of both patients; the lesions are larger, thicker and more numerous. The 4 year old boy who is also presented has a keratotic lesion the size of a pea on one large toe. When I presented the patients I showed on a pedigree chart that in four generations twelve members of the family were affected with this trouble. With the appearance of the condition in the youngest child the number has increased to thirteen.

DR. G. D. ASTRACHAN: I disagree with Dr. Gross. Mal de Meleda differs from keratoderma palmare et plantare in the fact that the keratosis is not limited to the palms and soles but spreads to the dorsal parts of the hands and feet and to the forearms and legs.

DR. SAMUEL FELDMAN: My opinion is that mal de Meleda and keratosis plantaris et palmaris are not the same. The former is not limited to the palms and soles but is present on other parts of the body. The condition of the patients presented tonight is ordinary familial keratosis.

GENERALIZED PIGMENTATION DUE TO CARCINOMA OF THE STOMACH. Presented by DR. CHARLES WOLF.

This man, aged 65, entered the Morrisania City Hospital on March 25, 1935, with the following complaints: dull, burning substernal sensation, attacks of vomiting immediately after the ingestion of meals, especially of solid food, anorexia, loss of 25 pounds (11.3 Kg.), weakness and generalized pigmentation of three weeks' duration.

There were marked cachexia, a generalized pigmentation over the unexposed portions of the body, a right inguinal hernia and an anterior bowing of the left tibia. Roentgenograms of the chest showed normal conditions; those of the tibias showed decreased density and thickening, as in Paget's disease, and those of the skull showed small areas of decreased density but no thickening or cotton ball appearance. The process was regarded as suggestive of a neoplasm. Fluoroscopic examination of the esophagus gave negative results; a series of roentgenograms of the gastro-intestinal tract revealed constant irregularity of the lower portion of the esophagus with retention and a constant irregular filling defect in the upper portion of the fundus of the stomach characteristic of malignant disease. The examination of the urine gave negative results. The blood count showed moderate anemia and no leukocytosis. The examination of the stool showed a 4 + reaction for blood. The Wassermann reaction of the blood was 4 plus. Examination of the chemical composition of the blood showed 75 mg. of sugar per hundred cubic centimeters.

DR. ADOLPH ROSTENBERG: This case is interesting, and I suggest the diagnosis of acanthosis nigricans. In a similar case under my observation there were warty excrescences in addition to the pigmentation. I believe that eventually warty lesions will develop in this case also.

DR. PAUL GROSS: The important thing in this case is to state what the condition is not. It is not acanthosis nigricans or Addison's disease. There is a grayish-brown pigmentation with some lichenoid changes of the skin and a mottled appearance. That is characteristic of a melanosis of Riehl. Apparently the carcinoma of the stomach has been responsible for the poor nutrition, which in turn led to the changes in the skin. This type of pigmentation was seen during the World War. It would be interesting to make a biopsy.

DR. C. LERNER: Although I did not see any definite warty thickenings as observed in cases of acanthosis nigricans, there were velvety patches suggestive of that condition. The pigmentation may be due to pressure on one or on both adrenal glands by the carcinoma.

DR. ISIDORE M. LASHINSKY: This patient has syphilis, and the question arises whether there is a relationship between the syphilis and the pigmentation.

DR. CHARLES WOLF: I do not think that in this case syphilis has anything to do with the pigmentation. It is more likely that the carcinoma is the underlying cause. The patient has metastases in the bones.

PSORIASIS (ECZEMATOID). Presented by DR. MARION B. SULZBERGER.

This man, aged 50, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, presents an eruption on the hands, wrists, side of the chin, popliteal spaces and left elbow of four months' duration. The patient had a similar condition ten years ago, which cleared up after four treatments with unfiltered roentgen radiation (75 roentgens weekly). Three years ago he had a somewhat similar condition on the hands and neck and was hospitalized for two weeks; the disorder improved after treatment with wet dressings and salves.

The present eruption started four months ago on the hands, sides of the neck, sides of the face and popliteal spaces. On the dorsa of the hands, ending abruptly just above the wrists, is an erythematous, scaly eruption. There is a typical psoriatic lesion on the left elbow. There is a similar less severe eruption in both popliteal spaces. On the neck and chin is a diffuse erythematous eruption. There is some ungual hyperkeratosis of one finger. Intradermal injections of oidiomycin and trichophytin gave negative results.

DISCUSSION

DR. DAVID SATENSTEIN: I think that as the study of psoriasis advances the entire conception of the disease will have to be changed. I am convinced that many other clinical conditions will be included in the group of psoriasis. The pathologic picture naturally varies according to the period at which the tissue is examined.

DR. PAUL GROSS: This patient undoubtedly has psoriasis. Apparently he has a dermatitis on the hands, in the cubital spaces and on the sides of the neck which has undergone a transformation into psoriasis.

DR. MARION B. SULZBERGER: I agree with Dr. Gross that psoriatic lesions could supervene on areas affected by any other cutaneous eruption. I believe that this patient has had a localization of psoriatic lesions at the site of two patch tests—one with trichophytin and the other with oidiomycin. It seems that this is simply a form of "isomorphous irritant effect" which is not uncommon in cases of psoriasis and was first described by Köbner.

CHRONIC URTICARIA. Presented by DR. MARION B. SULZBERGER for DR. ADOLPH ROSTENBERG JR.

This patient, who is from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, had reacted to crab meat, egg white, cat hair, dog hair, goose feathers, orris, chicken feathers, duck feathers, horse dander, rabbit hair and sheep wool. She also gave positive transfers to orris, mixed epidermal substances, mixed feathers and crab meat.

The patient's diet was restricted to the substances to which she reacted negatively, and she was given intradermal injections once a week of 0.1 cc. of a 1:100 dilution of mixed inhalants containing cat hair, dog hair, goose feathers, duck feathers, mixed feathers, rabbit hair, silk and wool, orris, flaxseed, horse dander, cattle hair, tobacco, chicken feathers, kapok, cottonseed, Pyrethrum and dust.

Formerly attacks occurred about once daily. At present the attacks of urticaria are infrequent and the patient feels a marked subjective improvement. This patient was presented at the meeting of this society in March (this issue, p. 372).

DISCUSSION

DR. ADOLPH ROSTENBERG JR.: The reason for presenting this patient at this time is that considerable improvement has occurred under the regimen outlined in the presentation.

DR. MARION B. SULZBERGER: It seems to me that at present this is the only feasible method to check the meaning of cutaneous tests in cases of chronic urticaria in which such tests show a multiple hypersensitivity directed toward foods and other substances, including inhalants. The foods can be eliminated but not the inhalants. Therefore, the logical steps are to eliminate foods and to try to desensitize the patient against the inhalants which have caused positive cutaneous reactions. I should not like to draw any conclusions from this report on one case, although the procedure employed has been followed by rapid improvement and the condition was of long standing.

ATROPHIA STRIATA COMPLICATING A DISSEMINATED NEURODERMATITIS. Presented by DR. EUGENE F. KELLEY.

This young woman states that she is troubled with recurrent plaques on the neck, cubital fossae and groin. The present eruption began ten weeks ago during an attack of the grip and rapidly became generalized. Two weeks after the eruption began there were pigmented erythematous lichenified lesions on both upper eyelids in the cubital fossae and on the upper and inner aspects of the thighs and vulva; there was also a large lesion encircling the neck. On the face, trunk and extremities were numerous discrete and grouped papules the size of a pinhead. There were superficial erosions and numerous marks of scratching. Two weeks later edematous and exudative lesions appeared in the axillae and on the lower portion of the abdomen and thighs; on healing these lesions left linear atrophic scars of various size varying from flesh color to blue. The urine showed a trace of albumin. The Wassermann reaction of the blood was negative. The biopsy specimen showed neurodermatitis.

DISCUSSION

DR. MARION B. SULZBERGER: It seems to me that the so-called "linear scars" are areas in which pigment failed to form because of the damage due to previous scratching.

DR. EUGENE F. KELLEY: In about the fourth week of the attack exudative lesions developed in the axillae and on the abdomen and thighs. These lesions subsided and were replaced by linear scars.

SYRINGOMA. Presented by DR. GEORGE J. SPINNER.

S. T., a woman aged 35, complains of an eruption which has been present for the past six years. It began on the left side of the neck. Two years later lesions

appeared on the right side of the neck, about the eyes and on the eyelids. One year ago similar lesions appeared on the abdomen. The lesions are discrete, oval, smooth, soft, raised above the level of the skin and brownish or waxy, they vary in size from that of a millet seed to that of a split pea; occasionally grouping is apparent. There are no subjective symptoms. Dr. Feldman reported that the biopsy showed dilated ducts in the sweat glands, formation of large cysts, strands of epithelial cells protruding into the corium from the cyst wall, epithelial strands occurring free in the corium and the presence of more than one layer of epithelial cells in some of the sweat coils.

DETROIT DERMATOLOGICAL SOCIETY

G. Warren Hyde, M.D., *Recorder*

Regular Meeting, Ann Arbor, Mich., April 10, 1935

Clyde K. Hasley, M.D., *President*

Tabes Dorsalis. Mal Perforant. Presented by Dr. Udo J. Wile, Ann Arbor, Mich.

A man, aged 30, with no history of infection and no previous antisyphilitic therapy, has had complete incontinence during the past week. The patient has noticed the development of painless ulcers on the right foot during the past three months. He suffered a severe burn to the left tibia many years ago. The patient appears asthenic and older than the stated age of 30. The scalp is normal; the pupils do not react to light but react in accommodation; there is generalized lymphadenopathy. The heart and lungs are normal. The abdomen, liver and spleen are not palpable. The upper tendon reflexes are normal; the lower ones are absent. There is extensive scarring over the left tibia, and deep, painless ulcers are present over the right heel and anterior portion of the arch of the foot.

The Kahn reaction and the reaction of the spinal fluid were 4 plus. Roentgenograms of the foot showed involvement of the head of the second metatarsal bone. There is no evidence of a Charcot joint. Examination of pus gave negative results.

DISCUSSION

Dr. Chester Doty: On the left leg there is a great deal of scarring with pigmentation, which is probably due to a burn. Without reading the history regarding the condition on the left foot, I think that the ulcers may possibly be tuberculous rather than syphilitic.

Dr. B. F. Barney, Ann Arbor, Mich.: I think that this is a case of trophic ulcer following tabes.

Dr. George H. Belote: I was somewhat surprised that no one asked whether an examination for evidence of actinomycosis had been made, as my co-workers and I have been fooled on one or two cases of actinomycosis. However, we have not had time to culture the material as yet. We believe that the disorder is a trophic ulcer associated with tabes.

Kerion. Presented by Dr. Udo J. Wile, Ann Arbor, Mich.

Case 1.—L. S., a man aged 27, a farmer, says that three months ago a lesion that was quite pruritic developed on the left side of the face. The lesion enlarged and new ones developed until the entire bearded area was covered. The past history is irrelevant.

The patient is underdeveloped and appears older than the stated age of 27. About the bearded region he presents an extensive eruption which is made up of

many nodules and tumors. Many abscesses are noted, and there is some alopecia. Megalosporon endothrix and Megalosporon ectothrix have been demonstrated. Serologic tests gave negative results. Treatment has consisted of application of wet dressings, oral administration of iodide, roentgen irradiation and manual epilation.

CASE 2.—M. S., a man aged 56, a farmer, the father of L. S., says that six weeks ago an eruption developed on the face; later it spread to involve the wrists. The patient's son has had a similar type of eruption for three months. The patient has been taking care of his son while he has been at home. He states that there is no ringworm infection in his cattle. The past history is irrelevant.

The patient presents lesions over the face, temples and wrists. The lesions over the temples have a central clearing and peripheral spread. The lesions on the wrists are tumors the size of a half-dollar which are riddled with abscesses. M. endothrix and M. ectothrix have been demonstrated. Serologic tests gave negative results.

Treatment has consisted of application of wet dressings, oral administration of iodide and manual and roentgen epilation.

CASE 3.—J. C., a man aged 60, a farmer, says that about four months ago a lesion developed on the bearded region; the disorder spread rapidly. The lesions are pruritic, and the patient has noted many abscesses in the lesions. He is a farmer and had been treating his cattle for ringworm infection before the onset of his eruption. The past history is irrelevant.

The facial features are distorted by the eruption on the bearded region, which consists of granulomatous tumors and hypertrophic lesions riddled with abscesses. There are areas of alopecia and many short, broken-off hairs. The eyelids and eyebrows as well as the upper lip are involved. M. endothrix was demonstrated in hairs. Serologic tests gave negative results.

Treatment has consisted of application of wet dressings, oral administration of iodide and manual and roentgen epilation.

DISCUSSION

DR. LOREN W. SHAFFER: I do not think I can say much about these cases. Mycelial growth in the hair by direct growth with the moist chamber was an excellent demonstration. I think it is unusual to see three cases of that condition at one time. Not many cases of kerion are seen in Detroit, as the disease is not as common in the city as it is in the country. I was particularly interested in the lesions on the hands of the one patient. The granulomatous type of lesions can be of trichophytic origin.

DR. UDO J. WILE, Ann Arbor, Mich.: There are two or three things about these cases which I think are worth mentioning. The father and son have the more characteristic inflammatory type of the disease. In the father and son M. ectothrix was found; in the patient in whom the condition is worst, only M. endothrix. Another thing worth mentioning is that some years ago, when a slight epidemic broke out in the neighborhood, I sent a former member of my staff to examine the cattle. Most of the patients with kerion have only a slight loss of hair and a little scaliness around the nose. Usually it results from rubbing the lesion with sulfur and lard or with one of the coal tars used in treating cattle. However, they get well rapidly under treatment with wet dressings and roentgen and manual epilation. If the members think that these three patients look bad today I wish they might have had the opportunity of seeing them when they came in. The faces of L. S. and J. C. were swollen to almost twice the normal size. There were granulomatous masses. My co-workers and I have seen five or six patients with kerion this year. A complicating factor is that both L. S. and M. S. show cutaneous sensitivity to iodine. We are extremely handicapped in our treatment of these patients from that standpoint. Good results have followed application of wet dressings and manual treatment, and the condition is clearing up nicely. These patients are also sensitive to iodide taken internally. They have

been given epilating doses of roentgen rays to the bearded region and marked improvement in the amount of inflammatory reaction which was present there has resulted. The father, who had a much less inflammatory type of lesion, was given 290 roentgens of radiation. The lesions over the arms have been irradiated with 125 roentgens filtered through 1 mm. of aluminum, and a second dose will be administered to the lesions over the arm. I am told that patients are benefited by protein shock. We have given some of these patients typhoid vaccine, but we have never been able to convince ourselves of the value of that treatment. Perhaps it is interesting to note that the eruption grows with extraordinary rapidity and that it has been present for only two or three weeks. After the disorder starts it spreads rapidly.

DR. LOREN W. SHAFFER: I wondered about the value of protein shock in the treatment of infection due to Trichophyton.

DR. A. P. R. JAMES, Toledo, Ohio: I have observed two cases in farmers, both of whom resided in the same district. One had a temperature of 104 F., and there were great bullous masses. Rapid improvement followed the alternating use of wet dressings and a lysed staphylococcus protein. Later a small dose of roentgen radiation was given to stop the pruritus.

LICHEN PLANUS. Presented by DR. UDO J. WILE, Ann Arbor, Mich.

M. G., a man aged 37, says that two months ago a pruritic nodular eruption appeared over the extensor surfaces of the hands, the flexor surfaces of the wrists and the lower portion of the legs. One lesion also appeared on the lower lip. There is no history of other recent lesions on the mucous membranes. The patient had a chancre in 1917 and received antisyphilitic therapy. He had lichen planus twenty-five years ago. Over the aforementioned areas are seen violaceous angular flat-topped papules, some of which are confluent and hypertrophic, and many points and lines of excoriation. On the lower lip is an eroded bean-sized papule. On the buccal mucosa are leukoplakia-like patches. There are no penile lesions. Serologic tests gave negative results.

DISCUSSION

DR. HARTHER L. KEIM: I wonder whether other members of the society have observed that there seems to be a tendency toward hypertrophic lesions and not small angular papules such as were formerly seen.

DR. EMMET C. TROXELL: I agree with Dr. Keim. The economic situation has been the cause of that change. The patients treat themselves, and physicians see them at a later stage of the disease.

LICHEN PLANOPILARIS? Presented by DR. UDO J. WILE, Ann Arbor, Mich.

B. R., a woman aged 57, says that about fifteen months ago there developed over the body an eruption to which she has applied petrolatum. There is no pruritus. The past history is irrelevant. The patient is well developed and well nourished. She presents an eruption confined to the trunk and upper extremities. The eruption is for the most part confluent; however, discrete lesions are present. The eruption is follicular in distribution and consists of follicular papules surrounded by an areola of dark purplish erythema. There are many angulated flat-topped lichenoid follicular papules. A biopsy specimen is presented. Serologic tests gave negative results. The condition on the scalp was not present when the patient was originally seen. It is a recent development.

DISCUSSION

DR. GEORGE H. BELOTE: Textbooks mentioned only one case of lichen planopilaris. In addition to the flat top type of papules ordinarily seen there are keratotic and follicular lesions. A good share of these lesions have involuted, and there is no pigmentation such as is seen in cases of lichen planus. To me the most interesting portion of this eruption is on the scalp, and my co-workers and I have shown

patients with such an eruption repeatedly in this hospital with a diagnosis of lichen planus involving the scalp. I do not recall seeing a case of such extensive involvement and loss of hair as this patient exhibits. The eruption is a subvariety of the typical condition.

DR. HARTHER L. KEIM: What is the outcome in such cases?

DR. GEORGE H. BELOTE: This is the first case of this type that I have seen.

DR. UDO J. WILE, Ann Arbor, Mich: I do not even know whether the disease is lichen planopilaris. As Dr. Belote stated, only one short description of that disease is given in textbooks. I cannot regard the lesions of the scalp as lesions of lichen planus. Ordinarily lesions of lichen planus do not occur on the scalp. One ought to determine whether there are lesions of lichen planus on the scalp.

DR. GEORGE H. BELOTE: A biopsy of the lesions on the scalp has not been made. Those lesions have appeared recently.

DR. A. R. WOODBURNE, Grand Rapids, Mich.: It seems to me that scarring would be associated with lesions of the scalp. There is too much scarring to consider lichen planus as responsible for the lesions on the scalp.

PAPULONECROTIC TUBERCULID. Presented by DR. UDO J. WILE, Ann Arbor, Mich.

J. B., a woman aged 24, states that her condition began two years ago with the appearance of two asymptomatic "spots" on the face. There was no progression for six months; then the eruption gradually spread to the face, chest and upper portion of the back. During the past six months the patient has suffered from loss of energy, chronic productive morning cough without hemoptysis, occasional night sweats and suspected elevation of temperature during the day.

Two types of eruption are present: One, consisting of pea-sized papules and papulopustules, the majority of which show excoriated tops or necrotic plugs, involves the face, chest and upper portion of the back; there are a few scattered atrophic scars. The other consists of an erythematous plaque the size of a half-dollar on the nose; it is covered with a tightly adherent dry white scale. No distinct follicular plugging is present. Roentgenograms show diffuse tuberculosis with cavitation in the upper lobe of the right lung. The Kahn reaction was negative.

DISCUSSION

DR. G. WARREN HYDE: The lesions on the face looked to me like lupus erythematosus and those on the back like papulonecrotic tuberculid.

DR. ARTHUR E. SCHILLER: I cannot see any reason why if this is a tuberculid there cannot be a mixed type of lesions. There exists a toxic type of eruption which may take on a mixed form. I think there is a variety of lesions in this case.

DR. FRANK STILES, Lansing, Mich.: I think there are two types of lesions. The lesions on the scalp and some of the lesions on the face look like tuberculids. I believe that the lesions on the face and cheek are lupus erythematosus or lupus vulgaris. I think I should decide on lupus erythematosus.

DR. HOWARD J. PARKHURST, Toledo, Ohio: I think that the lesions on the nose are characteristic of lupus erythematosus while those on the eyelids, back and chest are chronic tuberculids.

DR. UDO J. WILE, Ann Arbor, Mich.: I presented this patient with a diagnosis of pulmonary tuberculosis, but it seems to me that the case is interesting from two or three standpoints. First, physicians who are seeing many cases of pulmonary tuberculosis are not familiar with this type of case. I have discussed it with persons in sanatoriums. The association of tuberculosis with lupus erythematosus is not a new observation. I remember a case I saw some time ago. I believe that this patient's eruption is a tuberculid because of the hematogenous infections of the skin. One woman whose case I recall did not know she had tuberculosis. She had lost much weight and strength; dyspnea was present, and she had a streaked sputum for some time. She had an extensive diffuse tuberculosis of the right lung with a cavity somewhere near the apex.

TUBERCULOSIS ORIFICIALIS. Presented by DR. UDO J. WILE, Ann Arbor, Mich.

W. H., a man aged 52, has had a lesion on the right side of the lower lip for ten months, but it did not trouble him until four months ago, when it began to get painful. There are no other complaints or history of hemoptysis. The patient is well developed but undernourished and emaciated; he exhibits on the right side of the lower lip an irregular punched-out ulcer the size of a dime. The base is fairly clean. Around the border there are several pinpoint-sized glistening yellow nodules. The lesion is relatively painless.

Roentgenograms show far advanced bilateral fibro-exudative tuberculosis with multiple excavations. Examination of the blood showed mild secondary anemia, 15,000 white cells and monocytosis. A biopsy specimen is presented.

DR. GEORGE H. BELOTE: I think there is little I can say about this case. The patient has far advanced pulmonary tuberculosis, and the microscopic picture is that of tuberculosis. Ordinarily these lesions of the lip or mucous membrane are tender or rather painful. From the original examination I thought that the lesion was a gumma rather than a lesion of tuberculosis.

DR. UDO J. WILE, Ann Arbor, Mich.: This patient did not know or care whether he had pulmonary tuberculosis. I think that he is ignorant. Dr. Belote points out that ordinarily these lesions are associated with laryngeal tuberculosis or with the last stages of tuberculosis. This is probably contact tuberculosis.

GRANULOMA ANNULARE. Presented by DR. UDO J. WILE, Ann Arbor, Mich.

E. K., a woman aged 49, has lesions over the hands and forearms. During the past two years the patient noticed an eruption developing over the hands, fingers and forearms. She has received no treatment, and the lesions have caused no symptoms. There is an elevated annular waxy lesion on the right palm. Similar lesions are present over the thumb and middle finger of the right hand. Many firm papules, some of which are annular, are present over both forearms. Serologic tests gave negative results. Roentgenograms of the chest showed minimal tuberculosis of the apex of the right lung.

DISCUSSION

DR. GEORGE H. BELOTE: I do not recall the history. I think that the case is interesting and that from the clinical standpoint there cannot be any doubt as to the diagnosis of granuloma annulare. However, I have never before seen papular lesions of this type extending up the forearm. I think that the case is interesting from that standpoint.

DR. LOREN W. SHAFFER: I agree with Dr. Belote. I should hesitate to make a diagnosis without a biopsy. The lesions are somewhat suggestive of lupus erythematosus, and the nodules are definitely of the infiltrated type.

HYPERPIGMENTATION AND MACULAR ATROPHY OF THE SKIN ACCOMPANYING SECONDARY SYPHILIS. Presented by DR. UDO J. WILE, Ann Arbor, Mich.

L. C., a man aged 28, suffered from paralysis of the lower extremities following consumption of Jamaica ginger five years ago. The patient states that he had a chancre one and one-half years ago followed by a secondary eruption. The eruption has persisted. The patient has received no antisyphilitic therapy. He has lost 35 pounds (15.9 Kg.) during the past five years. There are a paralysis of the lower extremities, generalized lymphadenitis and an eruption consisting of discrete lesions from the size of a pea to that of a 5 cent piece over the trunk and arms. The lesions present an atrophic center surrounded by a hyperpigmented border.

The serologic reaction was 4 plus; the reaction of the spinal fluid was negative.

DISCUSSION

DR. HARTHER L. KEIM: I agree with the diagnosis of this rare type of syphilid.

MYCOSIS FUNGOIDES. Presented by DR. UDO J. WILE, Ann Arbor, Mich.

G. M., a man aged 69, says that the present illness began in September 1932. The patient has been observed at the clinic from Jan. 6, 1933 to the present time. Diagnoses of sensitization dermatitis, pemphigus, dermatitis herpetiformis and lymphoblastoma have been made during that period. At the last entrance, on April 9, 1935, the patient had typical plaques of mycosis fungoides. At present there are generalized erythroderma, marked thickening of the skin and many points and lines of excoriation. There is one vesicle on the wrist. Eczematous plaques are present on the torso and thighs. There is a generalized adenitis.

The Kahn reaction was negative; roentgenograms showed no abnormalities. The results of examination of the blood were as follows: hemoglobin, 93 per cent; red cells, 4,680,000; white cells, 22,000; polymorphonuclears, 74 per cent; lymphocytes, 12 per cent; basophils, 1 per cent; monocytes, 10 per cent, and eosinophils, 3 per cent.

A biopsy specimen is presented.

DISCUSSION

DR. HARTHER L. KEIM: I do not recall having encountered a bullous eruption as a consort to the lymphatic types of lesions; if the condition is any of the generalized obscure disorders lymphoblastoma should be considered. I think it would be interesting to follow the blood picture as there is so much infiltration of the skin. I believe that the blood picture will change.

DR. GEORGE H. BELOTE: At one time this patient had bullae on the corneas, and I am not sure that the diagnosis of pemphigus was not made at that time. This type of lesion has been observed in cases of pemphigus. At times the eruption looks like pemphigus, and at times it looks like dermatitis herpetiformis. The diagnosis of granuloma fungoides was not considered in the earlier stages of the disease. I do not believe that cases of granuloma fungoides or pemphigus beginning with vesicular lesions have been observed in this country. I am told by Dr. Blumenthal that in the German literature such cases are reported.

BENIGN CYSTIC EPITHELIOMA. Presented by DR. W. G. SAUNDERS.

M. D., a Negress aged 19, has lesions which appeared near the middle portion of the face about ten years ago. The patient states that they came on quite suddenly and have spread gradually. None of them have broken down or ulcerated. They are situated on the nose, cheeks, upper lip, forehead and neck. The lesions are from the size of a pinhead to that of a pea, somewhat opalescent and firm to the touch. They seem to reach a certain stage and then remain stationary. There has been little change during the past year of observation. Several biopsies were made. The first lesion was removed from the forehead near the inner portion of the right eyebrow. It was the size of a pea and had undergone recent growth and change. It appeared malignant clinically, but there was no ulceration; it was pearly and was covered by some telangiectasia.

The report on a biopsy made on May 29, 1934 by Dr. C. I. Owen was as follows: The epidermis is intact and exhibits a proliferation of compact masses of dark-staining cells which vary in shape and size. The masses also vary in size and shape and are fairly well demarcated. The cells resemble basal cells of the epidermis and are in general small and deeply staining, with small nuclei. No pearls are present. The diagnosis is basal cell carcinoma.

On July 10, 1934, Dr. Owen gave the following report: The epithelium is slightly keratinized. Beneath this there are many discrete and coalescing areas of cells resembling basal epithelium of the skin. A few pearls are present, but they are superficial and apparently not a part of the tumor. The diagnosis is basal cell carcinoma.

On a biopsy made on Oct. 30, 1934, Dr. Owen reported as follows: The specimen is from the skin and contains many hair shafts. The epidermis is thin and slightly keratinized. In some areas it is entirely eroded. The cutis exhibits much small round cell infiltration, with a few polymorphonuclear cells.

No new growth is present, and I am unable to identify this as a specific variety of infection. The diagnosis is chronic dermatitis.

The report on a biopsy made on March 12, 1935 was as follows: The specimen is from the skin and exhibits numerous well demarcated islands of new growth in the cutis. These islands have a peripheral layer of cells closely resembling basal cells, and the remainder of them consists of solid masses of cells which also resemble basal cells but are less typical than those of the peripheral layer. The diagnosis is basal cell carcinoma.

DISCUSSION

DR. GEORGE H. BELOTE: When this patient was presented at a former meeting I suspected that the condition might be beginning cystic epithelioma. This microscopic picture associated with the clinical picture is a great surprise to me.

DR. W. G. SAUNDERS: I think all that is necessary for a diagnosis of benign epithelioma is to show particularly the relationship to the basal layer or hair follicle. I think that the cysts probably depend on the rapidity of growth, dipping down and cutting off fibrous tissue and forming a central portion and cyst. A few cysts were seen in the sections.

DR. LOREN W. SHAFFER: One must differentiate between benign epithelioma and benign cystic epithelioma.

DR. UDO J. WILE, Ann Arbor, Mich.: I think that the microscopic picture resembles that of a cellular nevus. The specimen does not look to me like benign cystic epithelioma. I think the microscopic picture fits in better than the clinical picture. I do not know how the diagnosis can be proved. The cysts may just have come out, but they look as though they have been present for a long time. I do not know whether they are nevi or multiple benign epithelioma. I think it may be worth while to send a slide to Dr. Weideman, in Philadelphia, and one to Dr. Montgomery.

DR. HARTHER L. KEIM: Dr. Weller made the diagnosis of basal cell epithelioma from the slide.

A CASE FOR DIAGNOSIS. Presented by DR. UDO J. WILE, Ann Arbor, Mich.

A., a girl aged 15, states that she has had lesions over the chest, shoulders, abdomen and legs for the past seven years. New lesions have appeared from time to time during that period. The lesions cause no symptoms; they vary in size from that of a pinhead to approximately that of a 5 cent piece. All the lesions are rather indurated; some are erythematous, and others approach the normal color of the skin. The urinalysis and serologic tests gave negative results. A biopsy specimen is presented.

DISCUSSION

DR. A. R. WOODBURNE, Grand Rapids, Mich.: Clinically the lesions are suggestive of sarcoid. Several granulomatous types of lesions may have this appearance. However, one lesion is dense with fibrous tissue. The section has much cellular reaction and lymphatic infiltration. I think the most tenable diagnosis is sarcoid.

DR. W. W. DEUMLING, Fort Wayne, Ind.: These lesions look like cutaneous neuroma. In a case of cutaneous neuroma resembling a keloid that I reported the picture exhibited by the sections corresponded to that in this case.

DR. UDO J. WILE, Ann Arbor, Mich.: The oldest lesions show an enormous increase in epithelial atrophy. The younger lesions show an interesting hyperplasia, in bundles, and it may well be that these are undivided nerve fibers. Frequently there is an absence of this. I do not know what the condition is. I thought it was a benign plastic tumor arranged in bundles.

DR. H. R. STEVENS: Clinically, these lesions look like a number of lesions that one frequently sees on various parts of the body, either single or in groups of two or three. They are small red elevated nodules, which I call fibromas.

CHICAGO DERMATOLOGICAL SOCIETY

MAX S. WIEN, M.D., *Secretary*

Regular Meeting, April 17, 1935

WILLIAM ALLEN PUSEY, M.D., *President, Presiding*

TUBERCULOSIS (HEMATOGENOUS) OF THE FACE. Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

This woman, aged 35, of American descent, gave the following history when she was first seen by us in July 1934: Nineteen years ago an eruption appeared on the face, and it has never completely disappeared since. The lesions were multiple papules; the patient says that at first they looked like "boils" and had a crusted center but that later they changed to what they are now, namely, firm and prominent brownish nodules, varying from about 0.5 to 1 cm. in diameter, some of them distinctly translucent, irregularly distributed over the whole face. This eruption started during the summer and was aggravated every summer after exposure to the rays of the sun, when the lesions became more prominent. Also, for many years in the summer erythematous patches developed on the exposed surfaces of the arms, which—in contrast to the nodular lesions on the face—disappeared completely toward the beginning of autumn, leaving only blotchy pigmentation. While the lesions on the arm burned and were pruritic, those on the face caused subjective symptoms only after exposure to the rays of the sun.

A biopsy specimen taken from a nodule of the face revealed the picture of Boeck's sarcoid.

General examination gave negative results; the Wassermann and Kahn reactions of the blood serum were negative; as a roentgenogram of the chest taken four years ago was reported to show normal conditions, roentgen examination was not repeated.

Correspondence with Dr. L. M. Wieder, under whose care the patient had been for some time, revealed that four years ago the facial eruption was fairly typical of disseminated miliary lupus and that at that time lesions suggesting erythema induratum were present on the lower portions of the legs.

The patient's skin was tested for sensitivity to ultraviolet rays, but the results were negative.

The patient was referred to her private physician with recommendations for treatment consisting of administration of neoarsphenamine, cod liver oil and viosterol, generalized ultraviolet irradiation and a Gerson diet.

When my co-workers and I saw the patient nine months later (April 1935) she had, on both cheeks only, a few of the large nodules previously described. Lesions of a different character had developed in the form of slightly elevated, small brownish papules irregularly distributed all over the forehead, suggesting lupus miliaris disseminatus faciei or rosacea-like tuberculid of Lewandowsky. On the lower part of the right cheek an indurated, brownish plaque (about 3 by 2 cm.) had formed. In addition, small papular lesions suggesting folliclis were present on the dorsa of both hands. The patient informed us that a shower of such lesions had occurred every spring for the last three or four years. The lesions usually disappear within from three to four weeks, leaving fine scars. The appearance of these lesions is usually accompanied by that of erythematous patches of dermatitis on the forearms and on the dorsa of the hands and fingers, as stated heretofore.

Sections are presented.

DISCUSSSION

DR. OTTO H. FOERSTER, Milwaukee: I have a vague recollection of having seen this patient about four years ago, at which time a diagnosis of lupus miliaris disseminatus faciei was made, which, the members thought, was substantiated by

biopsy. Also at that time there was definite Bazin disease as well as lesions resembling sarcoid. Apparently these tuberculous lesions are of hematogenous origin. Roentgen examination of the chest gave negative results. In addition, I recall that there was dermatitis of the arms which was apparently related to exposure to the sun's rays and recurred from year to year during the warm weather.

Dr. H. E. Michelson, Minneapolis: I think this is an unusual case of tuberculosis of the skin, showing that various types may occur in one and the same patient. The lesions on the forehead can be regarded as lupus miliaris disseminatus faciei; those on the arm look like sarcoid, and those on the lower portion of the leg morphologically are erythema induratum. These three types of tuberculoderma are closely related biologically. It is well known that lupoid and erythema induratum are classified with the indurative tuberculids while lupus miliaris disseminatus faciei is in a controversial position. Some authorities classify it with the tuberculids; others group it with lupus vulgaris. For my part, I think it should be classified with the more fixed types, for the lesions heal very slowly and the sensitivity tends toward the positive anergic side.

Dr. Franz Blumenthal, Ann Arbor, Mich.: I agree with Dr. Michelson. I think there are differences in the size of the lesions but the allergic state is the same, and two reactions are present, one in the cutis and one in the subcutis. I think that these two reactions are not often seen, but I do not know why.

Dr. William Allen Pusey: I think this case indicates the way these conditions could be consolidated and grouped together rather than separated into different entities.

Dr. Louis A. Brunsting, Rochester, Minn.: I wish to call attention to the new purified protein derivative of the tubercle bacillus which was described at length in the supplement to the *American Review of Tuberculosis* for 1934. This material is now available for general use and offers an opportunity for quantitative testing and a probable method of treatment in cases of the type presented here. In the process of preparation of the purified protein derivative there is left only the "skin-reacting" portion of the extract, which is said to be without antigenic properties. The first test with the weaker solution injected intradermally must be applied with considerable caution, and the cases must be selected carefully. One instance has come to my attention of a rather severe local, focal and systemic flare-up in a patient with erythema nodosum in whom all the usual precautions had been observed.

Syringocystoma. Presented by Dr. E. A. Oliver.

A woman, aged 29, states that at the age of 12 she used a cream for the removal of freckles which had the trade name of "Othene." Shortly afterward she noticed a few papules on her neck, and subsequently lesions of the same type appeared on the face and on the eyelids. There has been no apparent change in the size of the tumors since the onset, but the patient thinks that the lesions have increased slowly in number. There are no subjective symptoms.

There is nothing of importance in the patient's past history, but she states that a sister has the same type of tumors and that her mother had carcinoma of the breast.

The patient presents on the sides of the neck, on the chin and on the anterior surface of the chest a number of discrete, yellow papules which vary in size from that of a pinhead to that of a small split pea. They are only slightly elevated above the level of the skin.

The histologic picture is that of syringocystoma.

DISCUSSION

Dr. Ruben Nomland: I think that the lesions this patient presents on the eyelids are the flat lesions of syringoma, which are fairly common. If one looks for them one will find them often. Within the last two years my co-workers and I

have seen about a dozen of these cases involving the eyelids alone at the Central Free Dispensary, and biopsies, which were made in half of these cases, all showed syringoma. The lesions are flat white papules located on the upper and lower eyelids that look a little like xanthelasma, except for the size and color.

DR. CLARK W. FINNERUD: I think, as Dr. Nomland said, that the lesions on the eyelids are undoubtedly of exactly the same nature as those on the chest, that is, syringocystoma. As was learned from a half dozen or more biopsies from material at the Rush Medical College, only histologic study differentiates these lesions on the eyelid from tricho-epithelioma and certain other disorders. There is an unusually large number of cysts in this section.

DR. E. A. OLIVER: When I first saw this patient two weeks ago I made a clinical diagnosis of syringoma. The lesions on the neck then appeared much more yellow than those on the eyelid. A section was taken from the eyelid because my co-workers and I thought there would be less scarring if it were removed from that location.

AMYLOIDOSIS OF THE SKIN (LOCALIZED). Presented by DR. RUBEN NOMLAND.

This man, an Italian aged 55, was under observation for fourteen months because of a supposed lichen simplex chronicus of the right thigh of several years' duration. A few months ago he complained of intense pruritus of both legs, and simultaneously the lesions of lichen simplex disappeared.

There is an eruption over both legs. Over the tibia there are patches 15 by 6 cm. that cannot be called lichenified but are indistinct, brown and scaling. Only after application of oil to remove the effect of the scales can it be seen that these patches are studded with numerous papules about 1 mm. in diameter. On the outer side of the leg are patches with less scaling and consequently more distinct papules. All the papules are firm, only slightly darker than normal skin and about 1 mm. in diameter. A few similar papules are present at the upper part of the healed areas of lichen simplex chronicus. A few hyperkeratotic papules, which may or may not be amyloid, are present on the posterior surface of the thighs.

General examination revealed no abnormality. The Wassermann reaction, examination of the blood and urinalysis gave negative results, and a roentgenogram of the chest showed no abnormalities. The intravenous Bennhold test for generalized amyloidosis was negative; there was 20 per cent loss of congo red from the serum in one hour.

A biopsy was reported on as follows: Several papules were present in the section, some involving only one or two papillae. Even in the earliest there was marked hyperkeratosis. The amyloid infiltrate was present in the papillae only where it was deposited around the capillaries in small corpuscular bodies the size of a cell. In some of these there were remnants of nuclei. There was little perivascular infiltrate. The amyloid reacted red to methyl violet and yellow to Van Gieson's stain, showing positive reactions for amyloid. The reaction with iodine was negative. Wright's blood stain gave excellent differentiation of the amyloid, but that reaction is not specific. Acid orcein showed that the elastic tissue was absent in the papillae.

Subcutaneous injection of a 1.5 per cent solution of congo red did not stain the papules, but intracutaneous injection of the dye was followed by diffuse red staining of the skin, lasting sixty hours. After that time the amyloid papules could be seen as pale red lesions.

DISCUSSION

DR. F. W. LYNCH, St. Paul: This case is an interesting example of the localized form of amyloidosis of the skin not associated with systemic or general disease of any sort. In most cases localized amyloidosis is associated with local disturbance —nevi or malignant changes or, perhaps less commonly, inflammatory processes; in other cases the amyloidosis is regarded as primary. In this case there is a suggestion that the disorder may be secondary to lichen simplex chronicus in

that some lesions have involuted. One would not expect to find this in lesions entirely amyloid. Dr. Nomland's microscopic interpretation was interesting, particularly as to the manner of deposition of the amyloid. The opinion formerly held was that the amyloid is deposited between rather than within the cells, gradually compressing the cells and, though situated outside, taking the outline of the cell. Dr. Nomland's interpretation is interesting and may be entirely correct.

DR. UDO J. WILE, Ann Arbor, Mich.: I wish to thank Dr. Nomland for calling attention again to something which was probably overlooked. Since it was first called to my attention I have found one case of amyloidosis of the tongue. In this case the condition was iodiopathic and not associated with either tuberculosis or malignant changes.

DR. RUBEN NOMLAND: I believe that the type of amyloidosis which this man presents occurs in approximately one half or more of the reported cases of localized amyloidosis. However, I wish to exclude from that estimate the cases that are secondary to senile keratosis or the like. I think the condition is a primary amyloidosis of the skin, not preceded by any disease that has reached a clinical level. Lichen simplex chronicus was present on the thigh, but it has never been present on the leg where the eruption occurs. The amyloidosis has been present for only a few months, and so far as I know as early a stage and as small lesions have never been described. I think that considerable work shows that this type of amyloidosis is primary in the skin, but there is no explanation as to why it occurs. No etiology has been worked out. Apparently some primary change occurs in the skin before the amyloid lesions appear.

DR. WILLIAM ALLEN PUSEY: Were all the lesions on the legs amyloid, or was there some lichen simplex chronicus?

DR. RUBEN NOMLAND: I think the lesions on the leg were all amyloid, without exception.

Regarding the staining of sections I wish to mention some points which I was unable to find in textbooks. I think amyloid stains best with extremely dilute solutions of methyl violet. One can use gentian violet just as well, probably in dilution of 1:1,000, or less. The sections are mounted and studied in glycerin. However, methyl violet is a poor stain to use in studying the morphology of amyloid, and I found that Wright's blood stain is excellent and differentiates amyloid from the other tissue. The most interesting feature to me was the capacity of the amyloid to take up congo red and retain a slight red stain; this stain persisted for ten days in the lesions of this patient, and in those of the patient I presented previously the stain was retained for several months. In a case of systematized amyloidosis I had a result similar to that which Dr. Brunsting obtained last summer. There is a selective red staining of the amyloid nodules following subcutaneous or intracutaneous injection of congo red that may prove helpful in diagnosis.

DR. UDO J. WILE, Ann Arbor, Mich.: Do these localized amyloid lesions take up iodine as readily as the others?

DR. RUBEN NOMLAND: In none of the patients I have examined did the lesions take up iodine at all. I think the same thing is true in most of the cases of localized amyloidosis that are reported. The most characteristic and diagnostic test is that with methyl violet, which stains amyloid red.

A CASE FOR DIAGNOSIS (CHRONIC MULTIPLE ULCERATIONS OF THE BUCCAL MUCOSA). Presented by DR. JAMES H. MITCHELL.

This man, aged 60, was first seen on March 7, 1935, with a disorder of about three months' duration. The patient stated that the lesions followed a bite by new artificial teeth and that the region was tender at first but was so no longer. He is a moderate smoker.

When the patient was first seen there was an irregular ulcer with a yellowish tenacious membrane to the left of the midline of the mucosa of the lower lip below the vermilion border. There was considerable swelling of the entire lip. Several pinhead-sized satellite lesions were noted, and more had formed and healed since then. No palpable submental gland was present at any time.

Smears were negative for tubercle bacilli and for Vincent organisms. Cultures were insignificant. The Wassermann and Kahn reactions were negative. The number of leukocytes averaged about 11,000, and there were about 5 per cent eosinophils.

Two intravenous injections of neoarsphenamine have been given without apparent result. Roentgen therapy, consisting of 3½ filtered skin units, has made no definite impression. Radiation from a water-cooled quartz mercury vapor arc lamp and gentian violet have been used from the beginning. The general condition of the lip is improved, but one large ulcer persists, and new small lesions continue to break out and heal.

DISCUSSION

DR. M. H. EBERT: It would be difficult to make a diagnosis in this case without a biopsy, but I did think of the possibility of tuberculosis. Only recently a patient seen in Dr. Ormsby's office, a young man who was apparently healthy and had no lesions of tuberculosis, exhibited a small ulcer in the labial fold of the oral mucous membrane that had been present for some time. It differed from this patient's lesion in that along the border there were small papillary projections that suggested tuberculosis. It was probably not primary but occurred in a patient who had a tuberculosis complex some time before. In this case I should suggest a tuberculin test with purified protein derivative to see if any local reaction occurs, and then histologic study of a section.

DR. M. E. OBERMAYER: I cannot quite agree with Dr. Ebert, for I think that the lesions do not show any clinical characteristics of tuberculosis. The diffuse swelling of the lip is suggestive of chronic cheilitis, and the ulceration could be explained as secondary, due to chronic irritation, possibly from the artificial plate.

DR. M. H. EBERT: I think that the clinical appearance of the lesions has been changed by the local treatment with roentgen radiation which Dr. Mitchell mentioned. That would change the clinical appearance.

DR. H. J. PARKHURST, Toledo, Ohio.: If I understood the history correctly, in my opinion the clinical findings are suggestive of periadenitis mucosa necrotica recurrens.

DR. WILLIAM ALLEN PUSEY: This is one of the cases, not so common, in which a microscopic examination is necessary in order to make a diagnosis. The disorder appeared absolutely nondescript to me.

DR. JAMES H. MITCHELL: I considered two diagnoses. The first lesions I saw made me think of epithelioma; hence I treated them with filtered roentgen radiation. That had no effect and need not necessarily have any effect on epithelioma of that type. Periadenitis mucosa necrotica recurrens does not fit in with these lesions, according to Sutton's description. One lesion has persisted from the beginning. Other lesions have constantly formed and healed. A week ago the patient had quite a deep fissure on the right side. Today it is healed. Smears for Vincent organisms and acid-fast bacilli gave negative results. Neoarsphenamine had no effect. At present I have no diagnosis to offer.

MULTIPLE HEMORRHAGIC SARCOMA. Presented by DR. JAMES H. MITCHELL.

This patient was presented at the meeting of the Dermatological Conference of the Mississippi Valley on Jan. 20, 1934 (ARCH. DERMAT. & SYPH. **30**:278 [Aug.] 1934).

She was again presented at a meeting of the Chicago Dermatological Society on March 21, 1934 (ARCH. DERMAT. & SYPH. **30**:475 [Sept.] 1934).

She is presented today because of the first lesion which has appeared on the foot. When the patient was first seen this was a dome-shaped red vascular lesion on the outer margin of the sole. Following administration of an unfiltered skin unit of roentgen radiation the lesion has involuted to a marked degree.

HEMORRHAGIC SARCOMA (KAPOSI). Presented by DR. E. P. ZEISLER.

This Spanish Jew, aged 63, has been under treatment for syphilis for the past year; he has received chiefly bismuth, mercury and iodides. For the past month he had complained of a painful eruption on the soles and about the ankles.

There are firm, discrete, bluish nodules on the soles and infiltrated bluish plaques on the mesial aspects of the ankles. The patient also presents evidences of arteriosclerosis, syphilitic myocarditis and pulmonary emphysema, retinitis and a cataract.

Examination at the clinic for patients with peripheral vascular diseases showed the temperature of the lesions to be 30.2 C. (86.4 F.) and that of the normal skin from 26 to 28 C. (78.8 to 82.4 F.), a difference of from 2 to 4 C. (3.6 to 7.2 F.). The temperature of each of the smaller lesions was higher than that of the surrounding skin. Bürger's test was negative. The pulsation of the vessels was normal on both sides. There was no blanching of the lesions with the histamine test. The peripheral circulation was considered unusually good for a man aged 63, and except for the elevation of temperature of the lesions there were no significant findings.

The Wassermann reaction has varied from 1 to 3 plus, and the Kahn reaction was 4 plus.

The results of histologic examination of a section from one of the plaques were reported as follows: "The sections reveal foci of lymphocytes among which spindle cells are seen. These cells show no conspicuous variation in size, shape or staining quality. Lymphocytes and fibroblasts are found in the close vicinity of blood vessels. In the regions of cellular infiltration there is an abundance of reddish-brown pigment containing iron. These changes are also found in the subcutaneous tissue. The histologic diagnosis is an early stage of Kaposi's sarcoma."

DISCUSSION

DR. DAVID LIEBERTHAL: I am much gratified to see the beautiful result obtained from the treatment of the lesions of the hand. It is unusual to see so few and such small lesions in a case in which the condition has lasted for some time. One does not need any corroboration of the diagnosis by the microscope, for the clinical picture is classic.

DR. H. E. MICHELSON: One thing is certain, the chronology of Kaposi's sarcoma is not fixed. In some patients the lesions have a rather energetic start, then reach a certain stage, quiesce or even disappear and reappear later. In others a single plaque develops and then a gradual extension occurs. The slowness in the development of the lesions in Dr. Mitchell's case is not opposed to the diagnosis.

DR. E. P. ZEISLER: I should like to comment on the possible relation of the disease to syphilis, which this patient has undoubtedly had. There are on record several cases of Kaposi's sarcoma in which the disease developed in patients under treatment for syphilis. The only treatment this patient has received consisted of local application of mercury bichloride. Wallhauser reported several cases in which the lesions disappeared completely under the use of mercury bichloride in dilute solution.

DR. JAMES H. MITCHELL: When this patient was first presented a year ago in January 1934, the diagnosis was not accepted wholeheartedly. Dr. Michelson and I were almost alone in supporting it. The fact that lesions were present on the hands seemed to be against the diagnosis. Today I overheard several of the members express the opinion that the lesion on the foot is a plantar wart. I saw that lesion two weeks ago, after the patient had cut into it. It bled profusely, and the patient had difficulty in stopping the bleeding. The lesions on

the hand and on the foot have been treated with 1 unfiltered skin unit of roentgen radiation. The appearance has changed remarkedly since then. I still believe that Dr. Michelson was correct in his diagnosis, and I shall try to continue treating the patient as best I can.

RECKLINGHAUSEN'S DISEASE (IN MOTHER AND DAUGHTER). Presented by DR. E. A. OLIVER.

This woman, aged 39, states that her disorder has been present since childhood, gradually progressing to its present extent. She presents a generalized eruption of tumors varying in size from that of a pea to that of a walnut and a number of pigmented macules.

Her daughter, aged 10, has had the same disorder for three years; she presents a few small tumors, a few pigmented macules and a large tumor mass, about 15 by 8 cm., on the outer aspects of the lower third of the right leg. This lesion is soft, and a roentgenogram showed slight thickening of the cortex of the tibia.

DISCUSSION

DR. E. A. OLIVER: In Cockayne's book "Inherited Abnormalities of the Skin" there is an interesting article on Recklinghausen's disease. It is stated that in from 12 to 17 per cent of these cases sarcomatosis develops and the patient dies. The disease seldom affects more than two generations, and about 8 per cent of the patients who have the disease are feebleminded. I was not aware that sarcomatosis is as common an accompaniment of this disease as the figures quoted by Cockayne make it appear.

DR. H. E. MICHELSON, Minneapolis: A number of cases of this condition have been observed in Indians. Perhaps the race may have some influence.

DR. MAX S. WIEN: In the surgical service my co-workers and I saw a Negress with Recklinghausen's disease and a tumor in the right thigh. The tumor was removed locally and was benign. The patient was again hospitalized about two years ago because of a recurrence, and her leg was amputated and revealed a rapidly growing sarcoma.

DR. JAMES H. MITCHELL: Several years ago I discussed with Dr. Phemister a case I had observed; he told me of several cases of Recklinghausen's disease in which sarcomatous degeneration had occurred and asked what my experience had been. In the only cases I have seen since I left Dr. Ormsby's office sarcomatous degeneration has not developed as far as I know. I looked up the records and found that there was a history of Recklinghausen's disease in the immediate family of each patient but no history of sarcoma.

DR. UDO J. WILE, Ann Arbor, Mich.: I think there is no general tendency for tumors of Recklinghausen's disease to undergo sarcomatous degeneration. It is conceivable that a lesion if subjected to extraordinary trauma might undergo such change, but I believe that these lesions are essentially benign except when subjected to trauma which may change any tumor into a malignant growth. In none of the cases I have observed has there been a tendency toward degenerative change, and I think that there is no inherent tendency toward this in the tumor itself.

DR. F. W. LYNCH, St. Paul: About two years ago my co-workers and I had an opportunity to observe a boy 17 or 18 years of age with Recklinghausen's disease who had elephantiasis of the lower portion of the leg and ankle. In this boy myxosarcomatous changes developed throughout the aforementioned region.

DR. MAX S. WIEN: Dr. Jaffé gave the impression that this tendency toward sarcomatous change is generally recognized among pathologists.

DR. E. A. OLIVER: I hope the members will agree that this tumor in the girl's leg is a lesion of Recklinghausen's disease and not one of syphilis. Despite

a negative Wassermann reaction and negative findings in the spinal fluid, she has been treated in the clinic for patients with congenital syphilis. I believe that the tumor is part of the picture of Recklinghausen's disease, other symptoms of which are present. This may be the beginning of the condition which Parkes Webber has described as elephantiasis neuromatosa.

MULTIPLE NEVI. Presented by DR. M. H. EBERT.

A boy, aged 15, was presented before the society at the meeting in November 1933 (ARCH. DERMAT. & SYPH. **29**:765 [May] 1934).

There has been little increase in the actual number of lesions. However, many of the minute ones have attained considerable size. Some of the large ones have become definitely pigmented. Most of them have a more definitely nevoid appearance than when the patient was first presented.

DISCUSSION

DR. M. H. EBERT: The striking thing about this boy is the appearance of such a large number of tumors quite generally distributed over the body. At the time of the first presentation, about eighteen months ago, the lesions were extremely small and some of them were removed and examined histologically. I did not know what would happen, whether new tumors would continue to develop or whether some would become pigmented or would undergo other changes, but I think that the matter is settled now. At present the lesions are quite heavily pigmented, and there is no question about their being nevi clinically as well as histologically.

DR. S. W. BECKER: I was glad to be able to see this patient again, for when the tiny nevi were examined several months ago it was found that they were composed of groups of so-called clear cells, and each of these cells gave a positive dopa reaction. I presume that in view of the fact that some lesions are not pigmented some of the cells do not give the dopa reaction at present. It is also interesting to note that in the latest section there is no sign at all of the so-called nerve nevus which, according to Masson, is caused by disturbance of the sheath of Schwann. This type of purely cellular nevus is scarcely ever seen as a prenatal nevus; in prenatal nevi these nerve type lesions occur deeper in the tissue.

DR. RUBEN NOMLAND: Then in these cases the nevus always originates from the epidermis rather than from the nerve cell?

DR. S. W. BECKER: It originates from the clear cell rather than from the dermis. These cells are different from the palisade cells. The boy's lesions seem to show a benign neoplasia of the clear cells.

DR. M. H. EBERT: Some of the American workers, notably Foote, by using a modified Bielschowsky method have succeeded in demonstrating nerve fibers in some of the nevi of this type. I hope to make this type of stain, and it will be interesting to see whether there is a better nerve supply in the nevus than in the nearby skin. I think there is no question but that the lesions are derived from the clear cells, and they evidently are quite different from the ordinary basal cell. The *Abtropfung* of Unna is well demonstrated in the small lesions. The question to be determined is whether the clear cells are derived from the sheath of Schwann.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: There is a striking superficial resemblance between this patient's condition and that described by Montgomery and O'Leary as multiple ganglioneuromas of the skin (ARCH. DERMAT. & SYPH. **29**:26 [Jan.] 1934). In the latter instance crops of new lesions developed slowly and the old ones involuted to a certain extent. Histologically, of course, there is no comparison between the two conditions.

DR. M. H. EBERT: I am glad to hear this observation of Dr. Brunsting's, for when I first saw this patient I thought his lesions might be of the same type as those described by O'Leary and Montgomery.

ANGIOKERATOMA. Presented by DR. A. W. STILLIANS.

This patient was presented at the March meeting (ARCH. DERMAT. & SYPH. 32:687 [Oct.] 1935) with the diagnosis of epidermolysis bullosa. An attempt at formation of a bulla had resulted in a hematoma 0.5 cm. in diameter in the atrophic area on the left elbow. Both elbows show small atrophic areas without hyperkeratosis. Examination of the feet was made, according to Dr. Wile's suggestion, and a number of small nonhyperkeratotic angiomas were found, the longest being about 0.3 cm. in diameter; some of them were situated at the junction of dilated venules.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: I am more certain today than I was last month that these lesions are not epidermolysis bullosa but the result of some peripheral vascular change. The lesions on the foot are even more striking, I think, than those on the elbow. There are numerous telangiectases, and I think that the condition conforms closely to the description of the lesions seen in cases of angiokeratoma. There is a good deal of cyanosis in the hands; they are quite cold, and the patient says she suffers from cold hands and feet but not from frost-bite. There is no keratosis in connection with these lesions, but that is not necessary. The lesions are multiple and hemorrhagic and occur at sites of trauma in patients who suffer from vascular injury.

NEW YORK DERMATOLOGICAL SOCIETY

R. H. RULISON, M.D., *Secretary*

April 23, 1935

FRED WISE, M.D., *President*

TUBERCULID OF THE CHEEKS. Presented by DR. HOWARD FOX.

M. M. B., a school girl aged 19, has suffered from the present eruption for the past two years. As a child she suffered from cervical adenitis, diphtheria, measles and whooping cough. There is no family history of tuberculosis. The tonsils were removed several years ago. The eruption consists of patches on each malar region, the one on the left cheek being larger and much more prominent than the one on the right and measuring 2 by 1¼ inches (5 by 3 cm.). The patch on the right cheek is round and is 1½ inches (3.8 cm.) in diameter. These areas consist of discrete but closely aggregated slightly elevated dull red papules the size of a pinhead. On pressure with the diascope yellowish-brownish pigmentation is apparent. The lesions have always been dry and entirely devoid of subjective symptoms. No marks of scratching are present. There is a slight amount of acne vulgaris on the forehead and back, and there is a moderate amount of dandruff. Tests with tuberculin in dilutions of 1:1,000,000 and 1:100,000 were negative. A sedimentation test of the blood showed a rate of 32 mm. in one hour. A blood count showed 7,000 leukocytes, and a differential count showed 46 per cent polymorphonuclears, 35 per cent small lymphocytes, 9 per cent large lymphocytes, 3 per cent transitionals and 7 per cent eosinophils. The patient has received four intravenous injections of gold and sodium thiosulfate and four fractional doses of roentgen radiation at weekly intervals. She has received no benefit from this treatment. She is robust and apparently in good general health.

DISCUSSION

DR. HENRY H. WHITEHOUSE: I agree with the diagnosis of tuberculid.

DR. EDWARD R. MALONEY: I think the disorder is acnitis. I do not care whether it is called acne agminata or acne telangiectatica. It has all the earmarks of acnitis except that the lesions are not as large as the lesions in most of cases

of these conditions, but the eruption is grouped as the lesions in cases of this type are grouped. It is made up of small papules, some of which have crusts and others of which are dull red. They appear in the characteristic places in which acnitis appears, namely, on the cheeks and the chin and occasionally on the arms. I think that the diagnosis of acnitis or acne agminata or tuberculid is the correct one in this case.

DR. PAUL E. BECHET: The eruption seemed to me to be an active tuberculosis and not a tuberculid. If such a thing as a follicular type of tuberculosis cutis exists, it would accurately describe the condition of Dr. Fox' patient.

DR. GEORGE M. MACKEE: I think that the eruption represents either tuberculosis or a tuberculid. This can be settled by a microscopic examination. My tentative diagnosis is acne telangiectatica, which is a tuberculid.

DR. EDWARD R. MALONEY: Another name which has been given to this condition, by an English author, is follicular lupus. In some of these cases the disease is true tuberculosis. This was true in one of the cases of acne agminata which I reported, and it may be true in this case, but I think that until that is definitely ascertained it is better to adhere to the term tuberculid.

DR. FRED WISE: I agree with the last speakers, and I think that the case is interesting because there is a peculiar morphologic and clinical picture, one I do not remember having seen in any patient with or illustration of tuberculosis or tuberculids. The sharp circumscription of the patches is a feature which is not seen in cases of lupus follicularis disseminatus.

DR. HOWARD FOX: I am not surprised to hear these different expressions of opinion. I acknowledge that I am not able to make a diagnosis in this case, as I have been mistaken repeatedly in trying to differentiate between tuberculosis and tuberculid of the face. The diagnosis will, I think, have to be decided by histologic examination.

FOLLICULITIS DECALVANS ET ATROPHICANS (LITTLE). Presented by DR. PAUL E. BECHET.

W. J., a man aged 45, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, was presented before this society on Oct. 23, 1928 (ARCH. DERMAT. & SYPH. **19**: 514 [March] 1929). Since then the process has greatly extended; the areas affected are much larger, and the plugs have mostly disappeared. I have observed the condition grow steadily worse in the past six years, despite varied and active treatment. I am presenting again the patient to show the great progress made by the disease.

A CASE FOR DIAGNOSIS (ECZEMA? PAPULONECROTIC TUBERCULID?)). Presented by DR. PAUL E. BECHET.

A. F., a man aged 20, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has had for seventeen years a nondescript eruption on the arms, chest, abdomen, thighs and buttocks. His family history is irrelevant except for the fact that an uncle died of pulmonary tuberculosis. The eruption began as erythematous papules, which progressed to pustulation and then dried, forming a crust; this dropped off, leaving a small ulcerated area, which on healing left a depressed scar. Scattered generally over the arms, chest, abdomen and buttocks are numerous discrete, deep-seated purplish-red papules the size of a pea, which are firm to the touch. Some pustules can be noted, a few of which are crusted. There are numerous scarred areas from 0.5 to 1 mm. in diameter in the area of eruption. On the inner sides of the thighs there are numerous grouped superficial, erythematous, dry, scaly papules, which are intensely pruritic. The report on the microscopic examination was perivasculitis.

DISCUSSION

DR. GEORGE M. MACKEE: According to the patient's statement and the history, the individual lesions and patches have existed for many years. The disorder is not

an evanescent eruption. I should regard it as an eruption of the mixed type of parapsoriasis, that is, parapsoriasis en goutte and parapsoriasis en plaques.

(Dr. Edward R. Maloney, Dr. Frank C. Combes, Dr. Henry H. Whitehouse, Dr. Joseph J. Eller and Dr. A. Benson Cannon agreed with the diagnosis of parapsoriasis.)

Dr. Charles Mallory Williams: I agree with the diagnosis of parapsoriasis of the mixed type. The eruption is exactly like that described by Brocq.

Dr. Eugene F. Traub: The individual lesions suggest parapsoriasis, some areas are definitely lichenified, and for those a diagnosis of lichenified eczema, especially because of the pruritus, would be more fitting.

Dr. Paul E. Bechet: The only point against the diagnosis of parapsoriasis, unless this patient presents two distinct cutaneous conditions, is the scarring on the forearms. There are typical varioliform scars. One or two papules on the arm show central necrosis. Of course, the lesions on the legs certainly look like parapsoriasis. On the other hand, there are some pruritic lesions on the inner side of the thighs, and the patient scratches them all the time. They resemble neurodermatitis. The case is therefore puzzling.

Hidrocystoma. Presented by Dr. Eugene F. Traub.

B. B., a woman aged 46, born in Russia, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, presents a single lesion on the center of the left cheek, which, she states, has been present on and off for six years. According to the patient, a tiny spot appears and increases in size; after having reached a certain point it grows no larger but gradually recedes and disappears; the entire evolution takes from three to four months. At no time has a cyst ruptured and discharged, its spontaneous disappearance invariably occurring without rupture. The present lesion is of three months' duration, and it is somewhat over 1 cm. in diameter and is the largest lesion the patient has had. She is presented principally for therapeutic suggestions.

DISCUSSION

Dr. Howard Fox: I suggest that the fluid in the lesion be examined to determine whether it is serum or sweat. I should also like to know whether this patient is frequently exposed to excessive heat, as a cook would be. As to treatment, I think the best results would be obtained by roentgen therapy.

Dr. Eugene F. Traub: The patient does her own housework, but she is not exposed to excessive heat. In my experience it is rather unusual to see a single lesion or to see a lesion attain as large a size.

Dr. Fred Wise: I understand, according to a publication by Marchionini, that one can determine by means of ordinary litmus paper whether the content of a vesicle is sweat or serum.

Dr. George M. MacKee: Roentgen therapy has resulted in cures. There have been some recurrences and some permanent cures. The same is true of excision. One of the interesting features in this case is that there is no history of intermittent rupture. The lesion disappears spontaneously without discharging. I have seen cases like this before, and I have assumed that the lesions reached a certain point of pressure which caused absorption. I agree with the diagnosis. The lesion is the largest one I have seen.

A Case for Diagnosis (Lupus Erythematosus?). Presented by Dr. J. Frank Fraser.

A. W., a woman aged 22, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. One month ago the patient noticed a small round red spot on the left cheek; this grew rapidly. A new lesion then occurred on the right cheek and spread over the face. The patient

had recently used a new face cream and rouge. One year ago she had urticaria for three days.

Over the bridge of the nose and over both cheeks and upper eyebrows there are irregular, bright red, well demarcated, slightly elevated, nonindurated lesions from the size of a pea to that of a quarter. The lesions are confined mostly to the upper portions of the cheeks. There are no scales or patulous ducts. The rest of the body is free from eruption. After four biweekly injections of redoxon, a synthetic vitamin C preparation, no improvement has occurred.

The Wassermann test was negative; the Kahn test was 1 plus. The report on a biopsy gave a questionable diagnosis of lupus erythematosus.

DISCUSSION

DR. CHARLES MALLORY WILLIAMS: I agree with the diagnosis of lupus erythematosus. I should like to know whether any rise of temperature or any constitutional symptoms, which often occur in cases of acute lupus erythematosus, have been present. I have even seen mental symptoms in certain cases.

DR. J. FRANK FRASER: There is no rise of temperature, and there are no constitutional symptoms. The disorder may be of an early discoid type. A complete physical examination, including a blood count, will be made. Until the onset of this trouble, four weeks ago, the patient had been in good health. It is too early to see any of the classic signs of lupus erythematosus, such as atrophy and scaling. Histologically the picture is not sufficiently typical to justify a diagnosis.

DR. A. BENSON CANNON: The location and distribution are certainly suggestive of lupus erythematosus, but because of the purpuric and hemorrhagic character noticeable on the nose and edges of the mucous membranes and of the bright erythema I am inclined to believe that the case is one of acute disseminating lupus erythematosus. Because of the acute, inflammatory character of the condition, I should suggest treatment with soothing applications of boric acid or saline solution, rest in bed and a high caloric diet. I believe that the patient should have thorough physical and laboratory examinations in order to rule out the presence of any focus of infection.

DR. FRED WISE: Would Dr. Cannon be disinclined to give a gold or a bismuth preparation in a case like this?

DR. A. BENSON CANNON: I should not give injections of a gold or bismuth preparation for fear of causing a rapid dissemination of the lesions. The vascular changes noted over the nose and mucous membranes are indicative, I think, of some toxic condition.

DR. EUGENE F. TRAUB: I agree with Dr. Cannon. I think that the disorder is acute lupus erythematosus, although in location and distribution the eruption is of the discoid type. Local treatment with calamine lotion together with general medical measures will probably clear up this condition.

DR. HOWARD FOX: I agree with what Dr. Cannon has said about the necessity for the utmost conservatism in treating a condition like this. In this case it is difficult to make a distinction between the discrete and the disseminated type of lupus erythematosus.

DR. CHARLES MALLORY WILLIAMS: I wish to correct my statement. I was not thinking of the ordinary fixed type of lupus erythematosus at all but of the acute disseminated type, which in this case happens to occur on the face and to be associated with swelling, intense congestion and the presence of a sharp border.

ERYTHEMA TOXICUM BULLOSUM. Presented by DR. FRED WISE.

H. K., a schoolgirl aged 13, has had a generalized eruption of six weeks' duration, for the treatment of which she applied at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. The past history is irrelevant, except for the fact that the patient has had frequent attacks of sore throat.

The tonsils are infected. The eruption appeared suddenly about six weeks ago in the form of macules and papules and was accompanied by malaise. There was no history of ingestion of drugs. The skin exhibited numerous large vesicles and bullae, from the size of a pea to that of a walnut, scattered irregularly on the extremities and trunk. These were for the most part flaccid, and soon after their appearance the contents became turbid and the bullae ruptured, leaving sero-sanguineous crusts. The Nikolski sign was present, but the patient's general health was unaffected. The Wassermann, Kahn and Kline tests and patch tests with iodide and bromide gave negative results. Culture of the contents of bullae revealed Staphylococcus aureus; microscopic examination showed absence of eosinophils and a few neutrophils. The blood count showed 11,000 white cells, 3,600,000 red cells and 73 per cent hemoglobin. The differential count was normal. Eosinophils were absent.

DISCUSSION

DR. PAUL E. BECHET: I think that this case illustrates well the fallacy of a precipitate diagnosis in cases of these bullous conditions. because when this girl first came to the clinic she had a number of bullae arising from noninflamed skin. She had a definite Nikolski sign. There were no gyrate or annular lesions, only scattered bullae, which certainly resembled pemphigus. If it had not been for her age and the short duration of the disorder—six weeks—one would have been sure that the condition was pemphigus. The following week the patient had typical erythema toxicum bullosum, with annular and serpiginous lesions which she does not show tonight. This case proves that one should be cautious in diagnosing a bullous dermatitis, a fact well known to dermatologists yet important enough to again be emphasized.

DR. FRANK C. COMBES: I wish Dr. Wise would differentiate this condition from erythema multiforme bullosum of Hebra.

DR. HENRY H. WHITEHOUSE: I rather favored the diagnosis of erythema multiforme bullosum until Dr. Wise spoke of the Nikolski sign. I thought that sign was present only in patients with pemphigus. I should like to know whether the members have found the Nikolski sign present in patients with other conditions.

DR. JOSEPH J. ELLER: I think this is a case of erythema multiforme bullosum.

DR. EUGENE F. TRAUB: This is the type of case in which I believe it is important to study the patient carefully. No one would believe that the patient has pemphigus, and yet the bullae arise from practically normal skin, and if such bullae were seen in an adult, they would make one seriously consider the diagnosis of pemphigus. However, this patient is a young girl whose general health is not seriously affected by the condition, and after the disease has run an indeterminate course the patient will undoubtedly recover. A study as to the exact cause of this toxic process may give some information as to the etiology of pemphigus. I agree that this is a toxic type of eruption rather than an unusual form of erythema multiforme bullosum.

DR. FRED WISE: The differentiation between Hebra's erythema multiforme and this type of eruption is one that the Viennese school especially stresses. The true Hebra type of eruption almost invariably begins on the dorsa of the hands, appearing later on the feet and still later on the cheeks. It manifests circular lesions, which this patient does not have, and a play of colors, especially of the iris type. This type of condition with toxic bullous erythema seldom presents lesions of the iris type, nor has it the target-like lesions. The Viennese put the Hebra type of erythema multiforme in the category of "idiopathic" eruptions, whereas in the case of an eruption such as that exhibited by this patient one nearly always finds some definite toxic cause. This patient has a definite focus of infection in the tonsils. With regard to the Nikolski sign, it may be elicited in cases of Duhring's disease, of epidermolysis bullosa and of pemphigus and frequently in cases of bullous eruptions of toxic origin. In cases of Hebra's erythema multiforme the labial and the buccal mucosa are more likely to be involved.

DR. HOWARD FOX: The important point in this case is to determine whether or not the disorder is pemphigus. Further discussion is more or less academic.

DR. FRANK C. COMBES: Must lesions of the iris type be present in cases of erythema multiforme bullosum exsudativum?

DR. FRED WISE: The conditions illustrated as classic eruptions always have lesions of the iris type and circinate and target-like lesions.

ERYTHEMA TOXICUM BULLOSUM. LIVEDO RETICULARIS. Presented by DR. FRED WISE.

B. D., an unmarried woman aged 26, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, applied for the treatment of a bullous eruption, which first appeared three months ago. She is subject to hay fever. On Jan. 4, 1935, she was tested with ragweed, dust and dog epithelium allergens in a clinic for patients with hay fever. She also received injections of a stock vaccine for a "cold" in the head. On January 11, a vesicular eruption appeared on the face, trunk and extremities, which, according to the patient, first manifested itself within forty-eight hours after the first injection of vaccine. The patient states that despite this eruption injections of ragweed and dust allergens and "cold" vaccines were continued at intervals until March 29. The vesicular eruption increased in extent and became bullous.

There is a widespread bullous eruption affecting chiefly the face and extremities, and scattered bullae are present on the trunk. The lesions are tense and contain clear serum. There is moderate itching. A few urticarial wheals are interspersed among the bullae, which vary in size from that of a pea to that of a hazelnut. There has been no ingestion or injection of drugs.

The extensor surfaces of the arms and thighs present a well defined and conspicuous livedo reticularis, which has been present for several years.

The blood count showed a normal number of red cells, 50 per cent polymorphonuclear neutrophils, 47 per cent lymphocytes, 3 per cent mononuclears and transitionals and no eosinophils or basophils.

DISCUSSION

DR. CHARLES MALLORY WILLIAMS: One thing in this case reminds me of a case I observed many years ago. The patient was a woman who had been treated with injections of tuberculin for tuberculous iritis, and at the end of such a course of treatment erythema multiforme developed on the forearms. It ran its course for a few weeks, and the patient recovered. I do not know whether the disorder was due to the tuberculin or was idiopathic.

DR. J. GARDNER HOPKINS: I think it would be interesting to know whether the vaccine the patient received contained streptococci. In cases of rheumatic fever I have seen lesions which seemed to be typical of Hebra's erythema multiforme. Coburn and others studying rheumatic fever found that the injection of streptococcus protein into patients with bullous lesions reproduced the circinate lesions. The association of these eruptions with tonsillitis suggests strongly that they are of streptococcic origin. It would be interesting to know whether in this case the eruption was elicited by injection of streptococcus vaccine.

DR. FRED WISE: Does the "cold" vaccine used for injections contain streptococci?

DR. J. GARDNER HOPKINS: Yes, those vaccines usually contain streptococci.

DR. FRANK C. COMBES: I think that the theory of a foreign protein as an etiologic agent is plausible. Similar conditions occur after administration of vaccine virus. I think that a few years ago Dr. Fox presented a patient with erythema bullosum following administration of vaccine virus.

DR. HOWARD FOX: It is well known that bullous eruptions may follow the parenteral administration of foreign proteins. As this patient received at least three kinds of injections of foreign proteins before the appearance of the eruption, I think it is probable that the disease was caused by one of them.

DR. FRED WISE: My reason for presenting this patient is her belief that the eruption is caused directly by the intradermal injections. She believes that she would not have the eruption if she had not been given the vaccine.

A CASE FOR DIAGNOSIS (ATROPHIA CUTIS? EARLY ATROPHYING SCLERODERMA?). Presented by DR. FRED WISE.

S. M., a married woman aged 32, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, applied for the treatment of a cosmetic defect of the skin of the upper portion of the chest, which first appeared five years ago. The patient's general health is good; she had an ectopic pregnancy nine years ago and at one time suffered from inflammation of the gallbladder. The family history is irrelevant.

The entire upper portions of the chest and breasts present a glossy appearance accompanied by a faint degree of desquamation, the lesion as a whole resembling the terminal stages of a scleroderma which has undergone a barely discernible grade of atrophy. Palpation discloses no sensation of induration or other structural cutaneous changes. Throughout the affected area are scattered reddish, indistinctly outlined, slightly scaly macular lesions, which have partly coalesced to form non-elevated, glossy plaques, with a finely wrinkled surface.

Repeated examinations for fungi have given negative results.

DISCUSSION

DR. FRANK C. COMBES: I agree with the diagnosis of atrophia cutis.

IDIOPATHIC HEMORRHAGIC SARCOMA OF KAPOSI. Presented by DR. FRED WISE.

F. M., a married man aged 40, a Jew, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has had the present eruption for five years. His general health has been unaffected, and the family history is irrelevant. He was born in this country, and his parents were Russian Jews.

The eruption, which affects the backs of several fingers and toes, consists of firm, discoid, slightly elevated, moderately indurated, dark violaceous plaques. The skin of the left ankle and lower portion of the leg is studded with closely aggregated, hazelnut-sized, dark bluish to brown and violaceous nodules, which form a broad, indurated and edematous mass encircling the limb and causing a marked hypertrophy of the ankle and lower half of the leg. Some of the nodules have an "alligator-skin" surface. The sole of the left foot presents a flat plaque ½ by 2 inches (1.2 by 5 cm.) in diameter. The buccal mucosa is unaffected. The right lower extremity presents similar, but much less advanced, changes. The Wassermann and Kahn tests were negative. Microscopic examination confirmed the clinical diagnosis.

DISCUSSION

(The members unanimously agreed with the diagnosis.)

A CASE FOR DIAGNOSIS (ERUPTION DUE TO A DRUG?). Presented by DR. EUGENE F. TRAUB.

H. A., a man aged 42, born in Russia, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has had an eruption of six years' duration. Only the skin of the scrotum and penis has been involved. The patient complains of intense itching, and the eruption at times exhibits a profuse discharge of serum. At present the eruption is dry and shows several rounded patches of dark brown pigmentation with little or no erythema. While the patient has been under my personal observation the eruption has remained limited to the present areas, but he states that the position of the lesions has changed from time to time. Thorough questioning as to the ingestion of any medicine or drugs elicited a negative reply. When phenolphthalein was given there seemed to be a flare-up of the condition, but this may have been a coincidence, as the patient is subject to frequent exacerbations and remissions.

DISCUSSION

DR. JOSEPH J. ELLER: My impression is that this is an eruption due to a drug in spite of the patient's statements to the contrary.

DR. R. H. RULISON: I think the most likely diagnosis is that which Dr. Eller suggested, namely, an eruption due to a drug.

DR. FRED WISE: I agree that the disorder looks like an eruption due to aminopyrine or acetophenetidin, but I suppose one would have to exclude the possibility of erythroplasia. It is an exudative eruption that has persisted for six years with exacerbations and remissions.

DR. GEORGE M. MACKEE: Has the possibility of a fungous infection been excluded?

DR. EUGENE F. TRAUB: The patient was examined for fungi, but none was found. Whereas negative results of one examination do not absolutely exclude this possibility, it seems most unlikely that such an infection exists in this case. A biopsy was made in another hospital, but no information as to the results could be obtained, and perhaps it would be well to make another. My first impression was that the condition was an eruption due to a drug, but I have questioned the patient carefully and can elicit no history as to the ingestion of any type of medicine which would account for the eruption. The picture changes from day to day. Several days ago the eruption was dry and scaly. Tonight it is an exuding patch. I believe that lichen planus can be definitely ruled out, but it is possible that the eruption may be simply an eczema in a patient whose skin has a marked tendency to pigmentation.

DR. FRED WISE: I think that the diagnosis of an eruption due to a drug is correct. The French describe this as *verge noir* or black penis, a condition due to the ingestion of drugs such as barbital or to a complication in a patient with leukemia.

SYPHILIS. Presented by DR. J. FRANK FRASER.

D. C., a man aged 63, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He states that the condition appeared on March 1, 1935, but this is questionable. In the left alar region of the nose there is a widespread destructive process. The borders of the lesion are raised, hard and infiltrated, the edges being sharply cut. The alar cartilage, lateral cartilage and inferior turbinate bone have been destroyed, and there is an opening at the base, probably into the maxillary antrum. There is no pain.

The Wassermann, Kahn and Kline tests were negative.

DISCUSSION

DR. A. BENSON CANNON: I agree with the diagnosis. The case is interesting.

DR. J. GARDNER HOPKINS: The edges seem extremely hard, and there is little involvement of the skin, as one would expect in a gumma. Unless the section is cut in some peculiar way, I think the condition is a definite squamous cell epithelioma.

DR. HENRY H. WHITEHOUSE: Because of the short duration and the amount of destruction which has taken place in that time, I think that the process is malignant.

DR. J. GARDNER HOPKINS: I do not think that the duration as stated by the patient is correct, and it does not justify diagnosis of either syphilis or epithelioma.

DR. JOSEPH J. ELLER: I think that the condition is syphilis.

DR. FRED WISE: My impression is the same as Dr. Hopkins', to the extent that I should certainly exclude by every means the possibility of carcinoma. I think, as Dr. Hopkins does, that the patient's statements are not to be taken seriously, especially as made by a patient of this type. At first glance, I should have thought of carcinoma and not of syphilis.

DR. GEORGE M. MACKEE: In regard to the question of the microscopic appearance of squamous cell epithelioma, I have found it tremendously difficult to depend on microscopic examination alone in cases of this kind. I am reminded of Weidman's article which was published a few years ago. He found every feature of a squamous cell epithelioma in long-standing benign ulcers. There are cases on record in which epitheliomas became more malignant after arsphenamine had been administered. I suggest, therefore, that a therapeutic test be made with oral administration of potassium iodide and intramuscular injections of a bismuth preparation.

DR. J. FRANK FRASER: At first glance the section gives the impression that the lesion is a squamous cell carcinoma, but one must remember the fact that in a secondary acanthosis the squamous cells may show an increase in the chromatin content of the nuclei, mitotic figures and even rapidity of growth and still not be cancer cells. One can account for these changes which resemble a squamous cell epithelioma as an epithelial reaction to the process which is going on below in the corium. This is the picture one frequently sees in gumma, a picture of acanthosis as a secondary reaction to panarteritis. There is panarteritis in this case, with an infiltration of plasma cells and a perivascular infiltration of lymphocytes, and there are distinct areas of necrosis and obliteration of blood vessels. For these reasons it is more reasonable to conclude that the lesion is one of syphilis than to regard it as an epithelioma.

DR. FRED WISE: Could not the condition be both a syphilitic lesion and an epithelioma?

DR. J. FRANK FRASER: Cancers do develop on old syphilitic lesions, but the histologic picture in this case is not that of cancer. The section shows a normal type of epithelial cell. As for the duration, all the members thought that the man was mistaken, but he adheres to his statement as to the duration under cross-examination.

A CASE FOR DIAGNOSIS (TUBERCULOSIS VERRUCOSA CUTIS? TERTIARY SYPHILIS?). Presented by DR. PAUL E. BECHET.

T. B., a Negro aged 60, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has on the dorsum of the left hand numerous discrete hyperkeratotic and verrucous lesions which have been present for twelve years. The largest lesion is about 3 mm. in diameter. Several of the patches have coalesced to form large patches. On the palm, and covering a large part of it, is a warty, sharply marginated overgrowth. The patient states that he had a genital sore many years ago, for which he received no treatment. The patient applied for treatment at the clinic today; hence no reports on laboratory examination can be presented.

DISCUSSION

DR. EDWARD R. MALONEY: I think the condition is syphilis.

DR. GEORGE M. MACKEE: I cannot make an unequivocal clinical diagnosis in this case. The lesions may be due to either tuberculosis or syphilis, but the fact that they have been present for ten years without causing any destruction is opposed to the diagnosis of syphilis. There are features in favor of that diagnosis, such as the unilateral distribution, the circinate and nodular character of the lesions, etc. The color, duration, lack of ulceration and slightly verrucous character are in favor of the diagnosis of tuberculosis verrucosa cutis. I favor the latter diagnosis.

DR. FRANK C. COMBES: In spite of the long duration, clinically the lesions look more like manifestations of syphilis than of tuberculosis. However, I hesitate to make a definite diagnosis.

DR. HANS J. SCHWARTZ: I incline more toward the diagnosis of tuberculosis.

DR. HENRY H. WHITEHOUSE: What is the patient's occupation?

DR. PAUL E. BECHET: He is a farmer and has done various kinds of work.

DR. HENRY H. WHITEHOUSE: I favor the diagnosis of tuberculosis verrucosa cutis because of the duration and character of the lesions.

DR. JOSEPH H. ELLER: I favor the diagnosis of tuberculosis verrucosa cutis.

DR. A. BENSON CANNON: I think that the lesions are syphilitic. I have one patient who has had a similar eruption confined to one hand for fifteen years and another patient who has had the same type of lesions for eleven years. I think that the spontaneous healing with scarring and the lack of inflammation around the papules, as well as the lack of a definite warty character, are all more suggestive of syphilis than of the verrucous type of tuberculosis.

DR. CHARLES MALLORY WILLIAMS: I favor the diagnosis of tuberculosis. Of course, I am no more positive than any one else, but I find it hard to believe that a nodular eruption due to syphilis could exist in the thin skin on the dorsum of the hand for so many years without producing either ulceration or atrophy. It may, but that is hard to conceive. Syphilis of the palm, I think, would not produce that curious mottled area with agglomerate, close-set punctate lesions. In my opinion, it is not characteristic of syphilis at all and may well occur in tuberculosis.

DR. R. H. RULISON: I think that the disorder is tuberculosis.

DR. HOWARD FOX: This case is similar to the one in the patient I presented at the last meeting. I agree with Dr. MacKee that the long duration is in favor of the diagnosis of tuberculosis, but I think that the appearance is somewhat suggestive of syphilis. The diverging opinions show the difficulty of making a clinical diagnosis.

DR. EUGENE F. TRAUB: I agreed with the diagnosis of syphilis in the case of the patient presented last month to whom Dr. Fox referred, but in this patient's case the evidence seems rather to favor tuberculosis.

DR. FRED WISE: I agree with Dr. Williams that everything in this case points to tuberculosis rather than to syphilis, especially the features brought out by Dr. Williams in regard to pitting of the palm.

DR. PAUL E. BECHET: I think the patient has more than pitting on the palm. He has a regular warty overgrowth, which is quite extensive, and this, of course, does not usually accompany syphilitic manifestations. His eruption also lacks the inflammatory redness that one ordinarily finds in syphilitic eruptions. For these reasons I am inclined to favor the diagnosis of tuberculosis. However, I shall report on the biopsy at the next meeting.

REPORT ON A CASE FOR DIAGNOSIS (SYPHILIS? TUBERCULOSIS VERRUCOSA CUTIS?). Presented by DR. EDWARD R. MALONEY.

V. H., a man aged 39, was presented before this society on March 26, 1935 (ARCH. DERMAT. & SYPH. **33**:195 [Jan.] 1936) for diagnosis.

The report on the biopsy is syphilis.

REPORT ON A CASE FOR DIAGNOSIS (PSORIASIS? MYCOSIS FUNGOIDES?). Presented by DR. J. FRANK FRASER.

R. G., a woman aged 29 years, was presented before this society on March 26, 1935 (ARCH. DERMAT. & SYPH. **33**:190 [Jan.] 1936) for diagnosis. The histologic picture was that of psoriasis. The case is now rapidly progressing into the tumor stage of mycosis fungoides, and the latest biopsy specimen shows the typical histologic picture of that disease.

LUPUS ERYTHEMATOSUS SHOWING MUTILATION OF THE EAR. Presented by DR. HOWARD FOX.

In view of some opinions expressed at the last meeting that the ear is rarely deformed by lupus erythematosus, a photograph is presented of a patient showing a striking deformity of the auricle. The patient, I. K., is a young man who has suffered for years from lupus erythematosus of the fixed type affecting the cheeks and ears.

Book Reviews

Clinical Diagnosis of Diseases of the Mouth. By Louis C. Hayes. With an introduction by Leo Winter. Price, $7.50. Pp. 461, with 353 black and white illustrations and 12 colored plates. Brooklyn, N. Y.: Dental Items of Interest Publishing Co., 1935.

Most of the book is devoted to diseases of the soft tissues of the mouth, and consideration of the work is confined to this part. The reviewer regrets to state that the book is unsatisfactory. The subjects are considered too briefly to give the essential facts; the author's style is loose, and there is little system in his presentations. The title of the book is "Clinical Diagnosis," and yet even when a disease is considered systematically he takes up the etiology, symptomatology and treatment in about equal extent and does not as a rule consider the diagnosis specifically. In examining the book the reviewer has not found a single disease of which the reader could find the essential facts in this presentation. For example, under scurvy, which is considered in less than a page, there is no mention of the rôle of vitamins. Under agranulocytosis, which is given a little more space than scurvy, the only hint that the lesions of the mouth are merely a feature of a general disease is that its causes are from medicines "that affect the granulocytic centres in the bone marrow and produce a diminution of the granular white blood cells." Of the etiology of Fordyce disease the statement is made that it is "due to a granular change in the protoplasm of the cells or the blocking up of the minute sebaceous glands in the oral mucous membrane." These illustrations are picked at random.

Curious mistakes occur: On page 1 of the table of contents one finds "excema," and on page 45, "cachezia," which from its context evidently is intended for cachexia. The author apparently uses the words that occur to him at the moment, without any thought of consistent usage. On page 158, under an illustration, one finds "tongue of syphilis," and under another illustration on the opposite page, "congenital lues."

Handbuch der Haut- und Geschlechtskrankheiten. By J. Jadassohn. Volume IX, Part 2. **Pyodermien Morbus Bang.** Price, 108 marks; bound, 116 marks. Pp. 512, with 137 illustrations. Berlin: Julius Springer, 1934.

This work is really one on the pus infections of the skin, to which 460 pages are given, while brucella infections of the skin are given 11 pages. One is rather surprised that 450 pages can be well devoted to a consideration of the pus infections of the skin alone, and yet the work justifies such elaborate treatment. The subject is covered in the utmost detail, including good bibliographies. It begins with chapters on the bacteriology of the pyodermas and one on the definition and differentiation of them by Professor Jadassohn and Professor Jessner of Breslau. To these general considerations 35 pages are given. Then in order are taken up all the various syndromes under which pus infections manifest themselves. The authors are well known dermatologists in Germany, and the various subjects have been treated with a thoroughness characteristic of this encyclopedia. The illustrations are beautiful. The chapter on brucella infections by Jadassohn comes up to the high standard of the work as a whole.

Haarkrankheiten und kosmetische Hautleiden, mit besonderer Berücksichtigung der Therapie. By R. O. Stein. Price, 12.60 marks, bound, 13.80 marks. Pp. 218, with 6 illustrations. Berlin: Julius Springer, 1935.

This work is in response to requests of physicians and students for publication of Stein's lectures on diseases of the hair and cosmetic defects of the skin. It is an interesting summary of the knowledge and practice in these fields. First,

diseases of the hair are considered in one hundred and three pages, and practically the same space is given to cosmetic defects of the skin. In the latter group are included nevi, tumors, scars and keloids, hyperpigmentation and depigmentation, anomalies of secretions of the sweat glands, anomalies of the sebaceous glands and angioneuroses. These are considered in detail, and the whole constitutes a convenient summary of knowledge and practice in these subjects of dermatology.

Diseases of the Skin. By Frank Crozer Knowles. Third edition, thoroughly revised. Price, $6.50. Pp. 640, with 240 illustrations and 11 plates. Philadelphia: Lea & Febiger, 1935.

The demand for this edition has given Knowles the opportunity to give the book a thorough revision. One third of it, he states, is absolutely new, and it has been enlarged by fifty pages. He has done a good job in bringing it up to date; at the same time, it retains its characteristics of a substantial, sound, practical exposition of the whole of dermatology. It has always been a good book and is one now. The fact that it is in the third edition is evidence of the appreciation which it has had and makes comment superfluous. The author may be congratulated both on its success and on the quality which has deserved it.

Modern Cosmetics, Formulation and Production. By Francis Chilson. Pp. 396, with 37 illustrations. New York: The Drug and Cosmetic Industry, 1934.

This is a book intended for use by the manufacturers of cosmetics and covers the technology of that subject. Its point of view is frankly commercial, yet it contains much valuable information for the dermatologist. It considers all the various forms of cosmetics, except solid toilet soaps, from face powders to depilatories, and contains much interesting information on the materials used in cosmetics and on their formulas. Chilson is evidently completely versed in the subject and writes with intelligence and honesty.

Books Received

Essays from the Clinic for Skin and Venereal Diseases at the State Medical Institute in Simferopol, Crimea. In Russian. Volume 1. Pp. 332. 1935.

Etude de la pigmentation dans les plaques peladiques. René Thée. Pp. 81, with 14 illustrations. Strasbourg: Ch. Roch, 1935.

Die Hautkrankheiten; ein Buch für Aerzte und Studierende. Dr. Richard Rohrbach. Price, 20 marks; bound, 21.50 marks. Pp. 393. Dresden: Theodore Steinkopff, 1935.

Directory of Dermatologic Societies *

INTERNATIONAL

NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY

American Secretary: Dr. Howard Fox, 140 E. 54th St., New York.

FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY
(CANADIAN BRANCH)

H. A. Dixon, President, Medical Arts Bldg., Toronto, Ont.
Norman Wrong, Secretary-Treasurer, Medical Arts Bldg., Toronto, Ont.
Place: Toronto, Ont. Time: May 1936.

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY

H. W. Barber, President, 7 Devonshire Pl., London, W. 1.
Louis Forman, Secretary, 7, Devonshire Pl., London, W. 1.

NATIONAL DERMATOLOGIC SOCIETIES

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Harry R. Foerster, Chairman, 208 E. Wisconsin Ave., Milwaukee.
J. Bedford Shelmire, Secretary, 1719 Pacific Ave., Dallas, Texas.
Place: Kansas City, Mo. Time: May 11-15, 1936.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.
Place: Kansas City, Mo. Time: May 11-12, 1936.

AMERICAN DERMATOLOGICAL ASSOCIATION

C. Guy Lane, President, 416 Marlboro St., Boston.
F. D. Weidman, Secretary, University of Pennsylvania, Philadelphia.
Place: New Ocean House, Swampscott, Mass. Time: June 4-6, 1936.

SECTIONAL DERMATOLOGIC SOCIETIES

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

H. G. Miskjian, President, 936 Rose Bldg., Cleveland.
E. W. Netherton, Secretary-Treasurer, 2020 E. 93d St., Cleveland.
Place: Cleveland. Time: Dec. 5, 1936.

NORTHERN NEW JERSEY DERMATOLOGICAL SOCIETY

Henry J. F. Wallhauser, President, Medical Tower, Newark.
Louis J. B. LeBel, Secretary, 165 Grant Ave., Nutley.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of January, March, May, September and November.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

J. W. Roussel, Chairman, 150 Baronne St., New Orleans.
Cornelius F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.

STATE DERMATOLOGIC SOCIETIES

CALIFORNIA MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, DERMATOLOGY AND SYPHILOLOGY SECTION

William H. Goeckerman, Chairman, 1680 N. Vine St., Hollywood.
Stanley O. Chambers, Secretary, 1210 Roosevelt Bldg., Los Angeles.

FLORIDA SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

J. L. Kirby-Smith, Chairman, 204 Laura St, Jacksonville.
W. M. Sams, Secretary, 310 Ingram Bldg., Miami.

LOUISIANA DERMATOLOGICAL SOCIETY

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, Maison Blanche Bldg., New Orleans.

MASSACHUSETTS MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Harvey P. Towle, President, 453 Marlborough St., Boston.
Rudolf Jacoby, Secretary, 270 Commonwealth Ave., Boston.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Louis Tulipan, Chairman, 224 E. 17th St., New York.
C. H. Peachey, Secretary, 197 S. Goodman St., Rochester.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA SECTION ON DERMATOLOGY

Abraham Strauss, Chairman, Medical Arts Bldg., Philadelphia.
L. G. Bembauer, Secretary, 5026 Jenkins Arcade Bldg., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

A. E. Schiller, Chairman, 10 Peterboro St., Detroit.
G. Warren Hyde, Secretary, 2501 W. Grand Blvd., Detroit.

MINNESOTA DERMATOLOGICAL SOCIETY

Hamilton Montgomery, President, Mayo Clinic, Rochester.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Marque O. Nelson, President, 307 Medical Arts Bldg., Tulsa.
Harry Green, Secretary, 1116 Medical Arts Bldg., Tulsa.

TEXAS DERMATOLOGICAL SOCIETY

J. C. Michael, President, 1215 Walker Ave., Houston.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Austin.

LOCAL DERMATOLOGIC SOCIETIES

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Dudley C. Smith, President, University of Virginia Hospital, Charlottesville, Va.
Francis A. Ellis, Secretary, 104 W. Madison St., Baltimore.

Bronx Dermatological Society

Eugene F. Kelley, Chairman, 93 Radford St., Yonkers, N. Y.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Samuel Hecht, President, 679 Greene Ave., Brooklyn.
Mortimer J. Cantor, Secretary, 907 St. Marks Ave., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo-Rochester Dermatological Society

Earl L. Eaton, President, 40 North St., Buffalo.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

Central New York Dermatological Society

George M. Fisher, President, 264 Genesee St., Utica.
Rudolph Ruedemann Jr., Secretary-Treasurer, 214 State St., Albany.

Chicago Dermatological Society

William A. Pusey, President, 7 W. Madison St., Chicago.
Max S. Wien, Secretary, 104 S. Michigan Ave., Chicago.

Cincinnati Dermatological Society

Samuel Goldblatt, President, 3208 Colerain Ave., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

H. G. Miskjian, President, 856 Rose Bldg., Cleveland.
E. W. Netherton, Secretary, 2020 E. 93d St., Cleveland.

Detroit Dermatological Society

L. W. Shaffer, President, 1553 Woodward Ave, Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

N. P. Anderson, Chairman, 2007 Wilshire Blvd., Los Angeles.
Thomas W. Nisbet, Secretary, 65 N. Madison Ave., Pasadena, Calif.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

Paul E. Bechet, Chairman, 55 Park Ave., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

Alberic Marin, President, 1414 Drummond St., Montreal, Canada.
Paul Poirier, Secretary, 2073 St. Denis St., Montreal, Canada.

New England Dermatological Society

William P. Boardman, President, 388 Marlborough St., Boston.
J. Harper Blaisdell, Secretary, 45 Bay State Road, Boston.

New York Academy of Medicine, Section of Dermatology and Syphilis

Max Scheer, Chairman, 509 Madison Ave., New York.
Frank C. Combes, Secretary, 80 W. 40th St., New York.

NEW YORK DERMATOLOGICAL SOCIETY

R. H. Rulison, Chairman, 114 E. 62nd St., New York.
Eugene F. Traub, Secretary, 140 E. 54th St., New York.

OMAHA DERMATOLOGICAL SOCIETY

Charles McMartin, Chairman, 611 City National Bank Bldg., Omaha.
Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Herbert J. Smith, Chairman, 3305 N. 17th St., Philadelphia.
Vaughn C. Garner, Secretary, Greene and Coulter Sts., Philadelphia.

PITTSBURGH DERMATOLOGICAL SOCIETY

Emerson Gillespie, President, 120 Tuscarawas St., Canton, Ohio.
Joseph J. Hecht, Secretary, 506 Medical Arts Bldg., Pittsburgh.

ST. LOUIS DERMATOLOGICAL SOCIETY

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

L. R. Taussig, President, 384 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.